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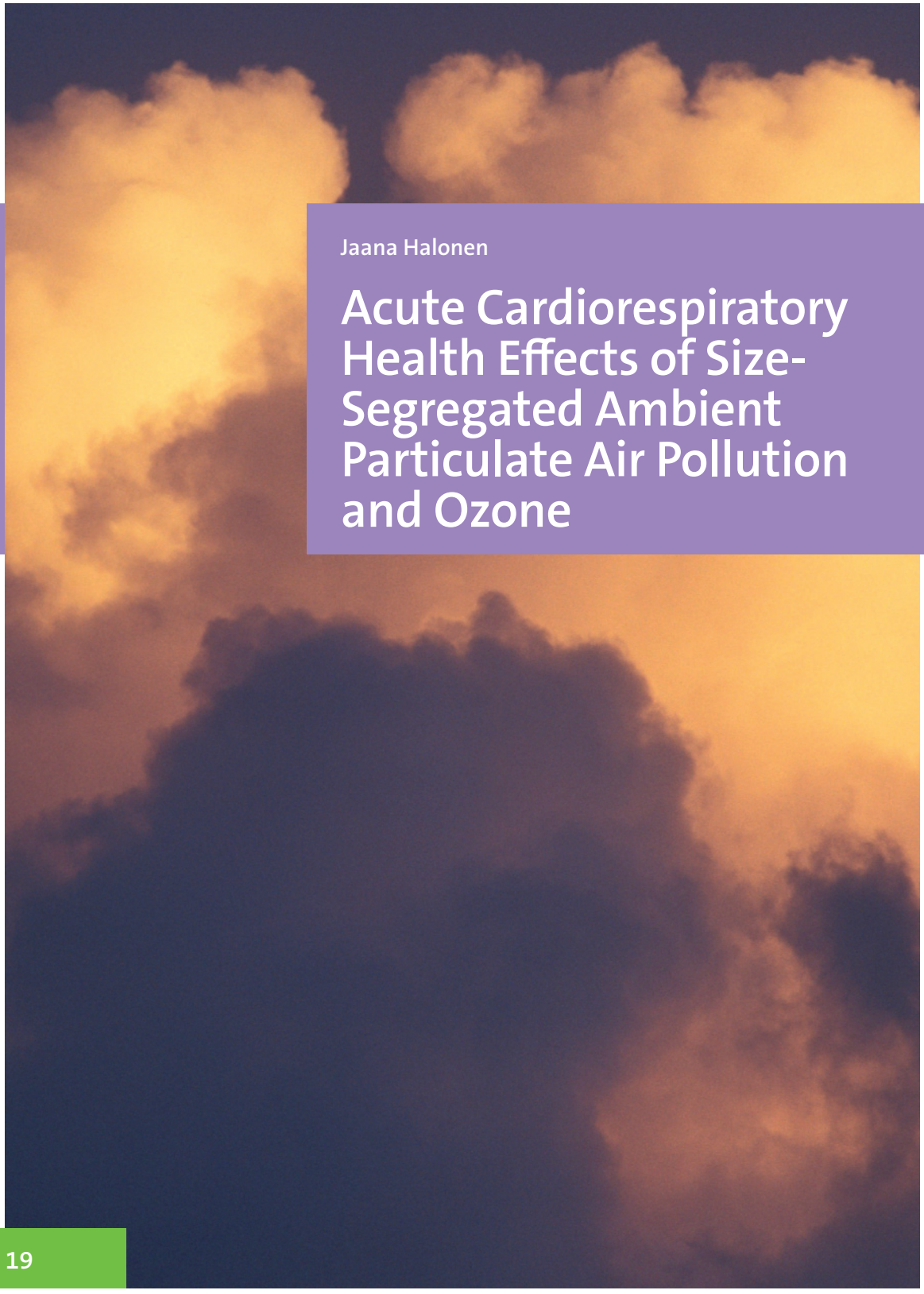

RESEARCH

Jaana Halonen

Acute Cardiorespiratory Health Effects of Size-Segregated Ambient Particulate Air Pollution and Ozone

Jaana Halonen

ACUTE CARDIORESPIRATORY HEALTH EFFECTS OF SIZE-SEGREGATED AMBIENT PARTICULATE AIR POLLUTION AND OZONE

A C A D E M I C D I S S E R T A T I O N

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ABSTRACT

Ambient air pollutants are one of the most harmful environmental stressors to human health. During the last decades, different ambient particulate and gaseous pollutants have been studied, and in numerous studies fine particles (<2.5 μm in aerodynamic diameter, $PM_{2.5}$) and larger, inhalable particles (<10 μm, PM_{10}) have been associated with excess morbidity and mortality. Particle size and composition are likely to affect the toxicity of particles. The composition of particles varies as they are emitted from different sources. However, the health effects of different types of ambient particles have rarely been determined because of the lack of measurement data.

The aim of this thesis was to study the components of ambient air pollution that may explain the short-term health effects associated with the changes in the levels of air pollution. Particles in different size fractions, gaseous pollutants such as ozone (O_3), nitrogen dioxide (NO_2), and carbon monoxide (CO), and $PM_{2.5}$ emitted from different sources were studied. The health effects studied were cause-specified daily mortality and hospital admissions for cardiorespiratory causes, and emergency room visits for asthma and chronic obstructive pulmonary disease (COPD). To establish possible differences in the sensitivity to air pollutants, the analyses were done separately for three age groups: children under 15 years of age, adults aged 15–64 years, and the elderly aged 65 years or older.

All the data was collected during 1998–2004 from Helsinki metropolitan area, which consists of four municipalities: Helsinki, Vantaa, Espoo and Kauniainen. Mass and count of ambient particles and concentrations of gaseous pollutants were measured at central measurement sites in Helsinki, except for O_3 that was monitored at a suburban station. Fine particulate mass ($PM_{2.5}$) was apportioned between four sources: traffic, long-range transport, soil, and coal/oil combustion. Daily mortality, hospital admission, and emergency room visit counts were obtained from national registers.

The mean (SD) daily levels of $PM_{2.5}$ in Helsinki were 9 (5.8) μg/m^3. More than half of the $PM_{2.5}$ mass was long-range transported, a fifth was from local traffic, and the rest was from soil, coal/oil combustion, and unidentified sources. The mean (SD) counts of ultrafine particles (UFP, <0.1 μm) and accumulation mode particles (0.1–0.3 μm) were 8 203 (5 137) and, 359 (261) 1/cm^3, respectively. The mean (SD) concentration of coarse particles (2.5–10 μm), NO_2, CO, and O_3 were 9.9 (8.3) μg/m^3, 28 (11.3) μg/m^3, 0.5

(0.2) mg/m^3, and 71 (20) µg/m^3, respectively.

Increases in daily levels of traffic-related pollutants (UFP, NO_2, CO) and O_3 were associated with increased asthma emergency room visits among children. Among the elderly, especially accumulation mode particles and $PM_{2.5}$, but also coarse particles, were associated with all respiratory, pneumonia and pooled asthma-COPD morbidity. Traffic-related and long-range transported $PM_{2.5}$, but also $PM_{2.5}$ from soil was associated with the respiratory morbidity of the elderly. Among children, the associations with ultrafine particles had a delay of 3–5 days, whereas among the elderly the associations were more immediate. Pooled asthma-COPD hospital admissions of the elderly were also increased in association with O_3. Few associations were observed among adults.

Overall, few associations between cardiovascular outcomes and ambient pollutants were observed. However, total cardiovascular and stroke mortality, but not stroke morbidity, among the elderly was associated with the increase in $PM_{2.5}$ during the warm season. There was also some suggestion of an association between arrhythmia admissions and $PM_{2.5}$.

The current results agree with earlier studies showing the effect of particulate air pollution and ozone on increased daily respiratory mortality and morbidity. Although few associations were observed for cardiovascular outcomes in the present study, these results together with results from earlier international studies and Finnish panel studies suggest the importance of particulate air pollution also in Helsinki, especially among individuals with underlying cardiorespiratory disease. Accumulation mode particles and $PM_{2.5}$ have more associations with different outcomes than other particle fractions. This may partly be due to better exposure assessment of these particles compared to ultrafine and coarse particles. Of the $PM_{2.5}$ sources, traffic and long-range transported $PM_{2.5}$ have the strongest effects on respiratory health, but also soil-derived particles seem to be harmful. Ultrafine particles and NO_2 are considered as markers of traffic pollutants, and in this study, it was not possible to identify the causal component of traffic emissions responsible for the observed effects among children. Overall, adults seem to be less sensitive to the effects of ambient pollutants than children and the elderly.

In summary, the effects of ambient pollutants are clearer on respiratory than on cardiovascular health, and among children and the elderly than among adults, in Helsinki. Although some differences were observed in the health effects of different particle size fractions and $PM_{2.5}$ from different sources, they all appear capable of causing adverse health effects. These results underline the importance of particulate matter together with ozone as a main environmental threat to health also in Helsinki.

Keywords; air pollution, cardiovascular, emergency room visit, epidemiology, hospital admission, mortality, respiratory, particulate matter, particulate number

Jaana Halonen, Kokoluokiteltujen ulkoilman hiukkasten sekä otsonin akuutit vaikutukset verenkierto- ja hengityselimistön terveyteen
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TIIVISTELMÄ

Ilmansaasteet ovat yksi haitallisimmista ympäristöaltisteista ihmisten terveydelle. Hiukkasmaisia ja kaasumaisia ilmansaasteita on tutkittu viimeisten vuosikymmenien aikana, ja useissa tutkimuksissa pienhiukkaset (läpimitta < 2.5 µm, $PM_{2.5}$) ja hengitettävät hiukkaset (< 10 µm, PM_{10}) on yhdistetty lisääntyneeseen sairastuvuuteen ja kuolleisuuteen. Hiukkasten koko ja koostumus vaikuttavat mahdollisesti niiden haitallisuuteen. Hiukkasten koostumus vaihtelee, koska niitä syntyy erilaisissa prosesseissa. Erilaisten hiukkasten terveyshaittoja on kuitenkin harvoin vertailtu, sillä niiden mittausaineistoa on ollut vähän saatavilla.

Tämän väitöskirjatutkimuksen tarkoituksena oli selvittää onko lyhytaikaisella altistumisella ilmansaasteille vaikutusta ihmisten terveyteen. Hiukkasia eri kokoluokissa, otsonia (O_3), typpidioksidia (NO_2), häkää (CO), sekä pienhiukkasia ($PM_{2.5}$) eri lähteistä tutkittiin erillisissä analyyseissä. Terveysvasteista tutkittiin kuolleisuutta ja sairastuvuutta sydän- ja verisuonitauteihin sekä hengityselinsairauksiin. Jotta eroja ikäryhmien välisessä herkkyydessä pystyttiin vertailemaan, analyysit suoritettiin erikseen kolmelle eri ikäryhmälle. Ikäryhminä analyyseissä käytettiin lapsia alle 15-vuotiaat, aikuisia 15–64-vuotiaat ja vanhuksia yli 65-vuotiaat.

Koko aineisto tutkimukseen oli kerätty vuosina 1998–2004 pääkaupunkiseudulta, joka kattaa Helsingin, Vantaan, Kauniaisen ja Espoon kaupungit. Hiukkasten massan ja lukumäärän sekä typpidioksidin ja hään mittaukset suoritettiin keskusasemilla. Otsonipitoisuuksia puolestaan mitattiin kaupunkitausta-asemalla. Pienhiukkasmassasta, $PM_{2.5}$, erotettiin neljä lähdettä: liikenne, kaukokulkeuma, maaperä sekä öljyn/hiilen poltto. Päivittäiset lukumäärät kuolleisuudesta, sairaalanotoista ja poliklinikkakäynneistä saatiin kansallisista rekistereistä.

Vuosikeskiarvopitoisuus (keskihajonta) $PM_{2.5}$ hiukkasille Helsingissä oli 9 (5.8) µg/m^3. Yli puolet pienhiukkasmassasta oli kaukokulkeutunutta ja viidennes oli peräisin paikallisesta liikenteestä. Loppu osuus hiukkasmassasta oli maaperästä, öljyn/hiilen poltosta sekä muista tässä tutkimuksessa tunnistamattomista lähteistä. Keskiarvopitoisuudet (keskihajonta) ultrapienille hiukkaselle (UFP, < 0.1 µm) ja akkumulaatio moodin hiukkasille (0.1–0.3 µm) olivat 8 203 (5 137) ja 359 (261) 1/cm^3. Keskiarvopitoisuudet (keskihajonta)

muille saasteille olivat; karkeat hiukkaset ($PM_{2.5–10}$, 2.5–10 µm) 9.9 (8.3) µg/m^3, NO_2 28 (11.3) µg/m^3, CO 0.5 (0.2) mg/m^3, ja O_3 71 (20) µg/m^3.

Tutkimuksessa havaittiin vahva yhteys lasten astman pahenemisen ja liikenneperäisten saasteiden (ultrapienet hiukkaset, NO_2, CO) sekä otsonin pitoisuuksien kohoamisen välillä. Yli 65-vuotiaiden joukossa akkumulaatio moodin ja $PM_{2.5}$ hiukkasten, mutta myös karkeiden hiukkasten pitoisuuksien noustessa kaikkien hengityselinsairauksien, keuhkokuumeen, sekä astman ja kroonisen keuhkoahtaumataudin (COPD) todettiin lisääntyvän. Lapsilla liikenneperäisten saasteiden haittavaikutus ilmeni 3–5 päivää altistumisen jälkeen, mutta yli 65-vuotiailla vaikutukset olivat nopeampia. Astma ja krooninen keuhkoahtaumatauti pahenivat yli 65-vuotialla myös otsonipitoisuuksien noustessa kesällä. Aikuisilla havaittiin vähän yhteyksiä terveyden ja ilmansaasteiden välillä.

Sydänsairauksien ja ilmansaasteiden välillä havaittiin vähän yhteyksiä. Kokonais-sydäntauti- ja aivohalvauskuolleisuus olivat yhteydessä $PM_{2.5}$ pitoisuuksiin lämpimänä kautena, mutta samaa yhteyttä ei havaittu sairastuvuudessa aivohalvauksiin. Sydämen rytmihäiriöiden ja pienhiukkasten välillä havaittiin myös heikko yhteys.

Tämä väitöstutkimus osoittaa, että ulkoilman hiukkaset ja otsoni aiheuttavat lisääntynyttä hengityselinsairastavuutta ja -kuolleisuutta myös pääkaupunkiseudulla. Vaikka sydänsairauksien ja ilmansaasteiden välillä havaittiin tässä tutkimuksessa vähän yhteyksiä, aikaisempien kansainvälisten tutkimusten ja suomalaisten paneelitutkimusten tulokset osoittavat, että hiukkasilla on merkitystä erityisesti hengityselinsairaiden sekä sydäntautipotilaiden joukossa. Akkumulaatio moodin sekä $PM_{2.5}$ hiukkaset ovat useammin yhteydessä hengityselinsairauksiin kuin hiukkaset muissa kokoluokissa. Tämä voi osittain johtua paremmasta altistuksen arvioinnista näille hiukkasille verrattuna ultrapieniin ja karkeisiin hiukkasiin. Liikenneperäiset ja kaukokulkeutuneet $PM_{2.5}$ hiukkaset aiheuttavat eniten terveyshaittoja, mutta myös maaperän hiukkaset ovat haitallisia. Ultrapienet hiukkaset ja NO_2 ovat liikennepäästöjen indikaattoreita, mutta tässä tutkimuksessa ei voitu erottaa yksittäistä liikennepäästöjen komponenttia, joka aiheuttaa havaitut terveysvaikutukset lapsilla. Aikuisväestö näyttää kaiken kaikkiaan olevan vastustuskykyisempää ilmansaasteiden vaikutuksille kuin lapset ja yli 65-vuotiaat.

Yhteenvetona voi todeta, että ulkoilman hiukkasten ja otsonin vaikutukset ovat voimakkaammat hengitys- kuin sydän- ja verenkiertoelimistöön sekä lapsilla ja yli 65-vuotiaila verrattuna aikuisväestöön Helsingissä. Vaikka eroja hiukkasten kokoluokkien ja lähteiden välillä havaittiin, niillä kaikilla näyttää olevan haitallisia terveysvaikutuksia. Tämän tutkimuksen tulokset osoittavat, että ulkoilman hiukkaset ja otsoni ovat merkittäviä ympäristöterveydellisiä uhkia myös Helsingissä.

Avainsanat; epidemiologia, pienhiukkaset, hiukkasten lukumäärä, hengityselinsairaus, ilmansaasteet, kuolleisuus, poliklinikkakäynti, sairaalanotto, sydänsairaus

CONTENTS

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ABBREVIATIONS

AIRGENE	Air Pollution and Inflammatory Response in Myocardial Infarction Survivors: Gene-Environment Interaction in a High Risk Group
APHEA	Air Pollution and Health: A European Approach (project name)
APHENA	Air Pollution and Health: A combined European and North American Approach (project name)
CAFÉ	Clean Air for Europe Programme
CO	carbon monoxide
COPD	chronic obstructive pulmonary disease
EMEP	Co-operative programme for monitoring and evaluation of the long-range transmission of air pollutants in Europe
EPA	Environmental Protection Agency
GAM	generalized additive model
HEAPSS	The Health Effects of Particles on Susceptible Subpopulations Project
HRV	heart rate variability
LRT	long-range transport
MI	myocardial infarction
NMMAPS	National Morbidity, Mortality, and Air Pollution Study
NO_2	nitrogen dioxide
O_3	ozone
PAH	Polycyclic aromatic hydrocarbon
PAPA	Public Health and Air Pollution in Asia (project name)
PEACE	Pollution Effects on Asthmatic Children in Europe (project name)
PEF	peak expiratory flow
PM	particulate matter
$PM_{2.5}$	(fine) particulate matter, aerodynamic diameter < 2.5 µm
PM_{10}	(ihalable) particulate matter, aerodynamic diameter < 10 µm
PMF	positive matrix factorization
TSP	total suspended particles
UFP	ultrafine particulate matter
ULTRA	Exposure and Risk Assessment for Fine and Ultrafine Particles in Ambient air Project
VOC	volatile organic compound

LIST OF ORIGINAL PUBLICATIONS

I. Kettunen J, Lanki T, Tiittanen P, Aalto P, Koskentalo T, Kulmala M, Salomaa V, Pekkanen J. Associations of fine and ultrafine particulate air pollution with stroke mortality in an area of low air pollution levels. *Stroke* 2007; 38:918-922.

II. Halonen JI, Lanki T, Yli-Tuomi T, Tiittanen P, Kulmala M, Pekkanen J. Urban Air Pollution and Asthma and COPD Hospital Emergency Room Visits. *Thorax* 2008; 63:635-641.

III. Halonen JI, Lanki T, Yli-Tuomi T, Tiittanen P, Kulmala M, Pekkanen J. Particulate Air Pollution and Acute Cardiorespiratory Hospital Admissions and Mortality among the Elderly. *Epidemiology* 2009; 20:143-153.

IV. Halonen JI, Lanki T, Tiittanen P, Niemi JV, Loh M, Pekkanen J. Ozone and Cause-specific Cardiorespiratory Morbidity and Mortality. Submitted.

1 INTRODUCTION

The harmful health effects of air pollutants were first described as early as in the 1930's after a fog episode in the Meuse valley, Belgium (Nemery et al., 2001). Increased mortality and morbidity counts were also reported after a fog episode in Donora, Pennsylvania in 1947 (Schrenk, 1949). However, it has often been referred that it was not until the famous London fog episode in December 1952 that truly awakened people for the hazardous effects of air pollutants. Increase in the short-term mortality in London after the fog episode was striking as had been the concentrations of ambient pollutants, and the link between pollution and mortality seemed obvious (Ministry of Health, 1954). Thereafter the pollutant levels decreased towards the late 1970's as a result of successful regulation actions. At that point, several investigators already concluded that there was enough evidence that low to moderate particulate pollutant levels did not affect human health (Holland et al., 1979). However, there were also other scientists who believed that even low particulate matter levels could have harmful effects on health (Pope and Dockery, 2006). More than a decade later their view was highlighted again when several unconnected epidemiological research groups found associations between rather low levels of particulate matter and mortality for cardiorespiratory diseases (Dockery et al., 1993; Pope et al., 1992; Schwartz and Marcus, 1990).

Today, the effects and risks of particulate matter and other air pollutants are still under vigorous examination. Recently, considerable effort was put into determining the risks of air pollutants in the Clean Air for Europe (CAFÉ) Programme (European Union, 2005). The CAFÉ Programme estimated that 1,300 premature deaths occur annually in Finland due to air pollutants. That is, in a country where the levels of pollutants are generally low. For Europe in total, the estimate was over 370,000 premature annual deaths because of air pollution. While mortality is the most severe outcome of the health effects of air pollutants, much larger population groups are suffering from milder effects that lead to reduced quality of life, increased morbidity counts, and higher costs of health care.

The air pollution research has continued for several decades already, but there still remains uncertainty about what are the most harmful ambient air pollutants, and where are they emitted from (WHO, 2007). One reason for the uncertainty is that the composition of ambient particles has changed over time because of changes in industrial development (Seinfeld and Pandis, 2006). Developed measurement devices have made it possible to investigate particles in different size fractions. The first particulate measures and air pollutants used in epidemiological studies were sulfur dioxide (SO_2), total suspended particles (TSP), black smoke, and inhalable particles (PM_{10}, diameter < 10 μm), whereas

coarse (PM_{10}–$PM_{2.5}$, 2.5–10 μm), fine ($PM_{2.5}$ <2.5 μm), and ultrafine (<0.1 μm) particles are nowadays the focus of research (Delfino et al., 2005; Donaldson and Stone, 2003; Hoek et al., 2000; Laden et al., 2000; Mar et al., 2000). Fine particles, $PM_{2.5}$, have already become the target of current air pollution regulations with a view to protect human health. However, toxicological studies suggest that ultrafine particles could be the most detrimental for health (Delfino et al., 2005; Donaldson and Stone, 2003; Valavanidis et al., 2008). Of the gaseous pollutants, NO_2 and CO have often been considered as markers of traffic-related pollutants, and not having independent health effects at the current levels, whereas the harmful effects of O_3 are biologically plausible (Bates, 2005; Brown et al., 2007; Gryparis et al., 2004; Hester and Harrison, 1998; Schwela, 2000).

Efforts to determine the health effects of ultrafine particles, have been made in Finland as part of the multi-city studies ULTRA (Exposure and Risk Assessment for Fine and Ultrafine Particles in Ambient air Project) (Pekkanen et al., 2000), HEAPSS (The Health Effects of Particles on Susceptible Subpopulations Project) (Lanki et al., 2006a; von Klot et al., 2005), and AIRGENE (Air Pollution and Inflammatory Response in Myocardial Infarction Survivors: Gene-Environment Interaction in a High Risk Group) (Peters et al., 2007; Ruckerl et al., 2007a) and also elsewhere (Andersen et al., 2008; Andersen et al., 2007a; Peel et al., 2005; Wichmann et al., 2000). There has also been a few chamber studies where healthy people have been exposed to particulate pollutants in controlled conditions (Samet et al., 2007). However, there has been a lack of long and good quality measurement data of particles in the ultrafine size fraction for epidemiological time-series or cohort studies (Englert, 2004). Fine particles have been more often measured and studied, and the main sources of fine particles are known. Fossil fuel combustion e.g. emissions from traffic and power plants, re-suspended dust from soil, wood and biomass combustion, as well as sea salt spray in areas close to sea shore are all sources for fine particulate matter (Seinfeld and Pandis, 2006). During the last decade, the health effects of source-specified particles have also been studied (Andersen et al., 2007b; Laden et al., 2000; Lanki et al., 2006b).

In Helsinki, the measurements for the size fractioned particles started already in the mid 1990's (Hussein et al., 2004b) when the new era of air pollution research had just begun. Together with regular air pollutant monitoring data this particulate measurement data enabled the examination of the short-term health effects of ambient particles in several different size fractions, and the effects of gaseous pollutants. Source apportionment for the fine particle mass, on the other hand, enabled the investigation of the health effects of fine particles, $PM_{2.5}$, from different sources. Thus this population level study is among the first that was able to use long-term continuous measurement data of the size-fractioned particles and mass of source apportioned $PM_{2.5}$, and also to link it to the excellent Finnish registers on health.

2 REVIEW OF THE LITERATURE

2.1 Air pollution

Air pollution can be defined as a condition in which the concentrations of substances in the atmosphere are high enough to cause measurable effect on man, animals, vegetation or materials. A "substance" here is any natural or anthropological airborne chemical element or compound that can exist in the atmosphere as gases, liquid drops or solid particles (Seinfeld, 1986). The most considerable sources of anthropogenic air pollutants are processes involving fossil fuel combustion such as energy production, traffic, and industry.

2.1.1 Size fractions and sources of particulate matter

When speaking of "particulate matter" we refer to substances that under normal conditions are in liquid or solid form in the atmosphere and that vary in size and density (Seinfeld, 1986). Particles under 20 μm in aerodynamic diameter are of special interest because they settle out slowly from the air (Koutrakis and Sioutas, 1996). Because the exact size of particles cannot be determined, they are usually considered as spheres and the measure "aerodynamic diameter" is used to describe the size of particles. Strictly speaking, aerodynamic diameter is the diameter of a sphere of unit density (1g cm^{-3}) that has the same gravitational settling velocity as the particle in question. Particulate matter is often classified particularly by the physical size of particles. Physical size refers to the above mentioned aerodynamic diameter of particles that varies from few nanometers to tens of micrometers. Many properties and atmospheric reactions of particles are predicted based on their size, the compounds they are formed of, and the size of their surface area (Seinfeld, 1986).

Ultrafine particles have diameter less than 0.1 μm. One sub-fraction of ultrafine particles is called nucleation mode (<0.01 μm). These particles are formed by gas-to-particle conversion, and condensation of hot vapors, but sometimes they are also directly emitted as particles from combustion processes. Nucleation mode particles have a short life span and they coagulate fast with each other to form larger particles, Aitken mode particles (0.01–0.1 μm) (Seinfeld and Pandis, 2006). In addition to formation via gas-to particle conversion, condensation and coagulation processes, ultrafine particles are also emitted directly as particles.

Ultrafine particles are derived from local emission sources such as traffic and fuel combustion in stationary sources (Colls J, 2002; Seinfeld and Pandis, 2006). Ultrafine particles contribute little to the particulate mass (Pekkanen and Kulmala, 2004), but they

are large in number and have high short-term peak concentrations. Therefore especially nucleation mode particles can make a considerable contribution to the short-term inhalable particle exposure. Aitken mode particles have lower peak concentrations than nucleation mode, but they are always present in the ambient air (Colls J, 2002; Seinfeld and Pandis, 2006). Besides having large number, ultrafine particles have also large surface area in relation to their mass. From the epidemiological point of view, large surface area means that there is more active area for particle-cell interactions in the airways, which is one reason why ultrafine particles are considered more toxic than larger particles (Donaldson and Stone, 2003; Sioutas et al., 2005). Another reason for the harmfulness of these particles can be their ability to penetrate deep into the airways. It has been demonstrated that particles in the size fraction of <0.1 μm would reach best the alveolar region of the lungs (Schulz, 2000).

Fine particles ($PM_{2.5}$, <2.5 μm) are emitted straight from combustion sources but they are also formed in the air via condensation of precursor gases onto existing particles, and via coagulation of ultrafine particles (Seinfeld and Pandis, 2006). The growth rate depends on the number of particles, their velocity, and surface area. The term "fine particles" is currently considered a synonym for the mass of particles less than 2.5 μm in aerodynamic diameter, $PM_{2.5}$. Slightly stricter size range, 0.1 μm to ~ 2 μm, defines a sub-fraction of fine particles that is also called accumulation mode (Seinfeld and Pandis, 2006). Fine and accumulation mode particles do not grow into larger, coarse, particles due to growth-limiting physical factors and therefore they are "accumulating" and lasting (Seinfeld and Pandis, 2006). Particles in the accumulation mode fraction are special in that they account for most of the ambient fine particle surface area (Hussein et al., 2004b; Seinfeld and Pandis, 2006).

Fine particles consist mainly of sulfate, nitrate, ammonium and secondary organics (Seinfeld and Pandis, 2006). Most of the particles are emitted from combustion processes using fossil fuel such as traffic and power plants. Other fine particle sources are waste incinerators, wood combustion, especially in residential areas where wood may be used as a secondary source of energy, and sea salt spray in the vicinity of sea (Colls J, 2002). Fine particles have low settling velocity that enables long life span and transportation of these particles over thousands of kilometers from the emission source (Spengler and Wilson, 1996). Therefore the total ambient particle mass is always affected by elsewhere produced fine particles as well as older particles. The composition of fresh and old particles may be different because of the conversion of particles through chemical processes that take place in the atmosphere (Seinfeld, 1986; Seinfeld and Pandis, 2006). Local combustion particles and long-range transported particles are therefore also defined as primary and secondary particles, respectively, and thought to probably have different health effects (Schwarze et al., 2006).

Generally, particles from 2.5 up to 50 μm are considered as coarse particles and they are mostly primary particles containing only some secondary sulfates and nitrates (Seinfeld and Pandis, 2006). In epidemiological studies, however, the diameter used for coarse particles is most often defined as 2.5–10 μm (PM_{10}–$PM_{2.5}$), because these particles are in inhalable size fraction, and may therefore have biologically plausible effects on health. These particles are formed by fragmentation of matter and in other mechanical processes such as wearing off roads (Colls J, 2002). Traction sanding gives also rise for the formation of coarse particles that are thereafter distributed by local winds. However, these particles are not transported far from their initial source because they are larger in size and heavier than combustion derived particles and therefore deposited faster. Both, the coarse and the fine fraction of particles contain also material of biological origin like bacteria, pollen, and fungal spores. However, the major part of such intact bio-aerosols occurs in the coarse mode, and in deposited and re-suspended dust, particles of biological origin may be abundant (Monn, 2001).

2.1.2 Ozone and other gaseous air pollutants

Ozone (O_3) is a known irritant gas in the troposphere. Ozone is a reactive, light blue and piercing smelling gas that is formed as a secondary pollutant in conditions where nitrogen oxides, volatile organic compounds (VOCs), and sunlight are present (Bernstein et al., 2004; U.S.EPA, 2006). In the rural areas, ozone formation occurs also with the help of methane that derives from rice fields, domestic animals, and dumping grounds. Simplified equations that regulate the ozone concentrations are as follows. First, nitrogen dioxide is dissociated into nitric oxide and atomic oxygen with the help of sunlight:

$$O_2 + h\upsilon \rightarrow NO + O$$

Where in hυ h is Planck's constant and υ is the frequency of light. Atomic oxygen then combines with molecular oxygen to form ozone:

$$O + O_2 \rightarrow O_3$$

If the photostationary cycle described above is altered by events consuming nitric oxide or favoring the production of nitrogen dioxide, the formation of photochemical pollution takes place. The cycle is most often altered by reactions between nitric oxide and atmospheric peroxides (RO_2) that lead to the formation of nitrogen oxide:

$$NO + RO_2 \rightarrow NO_2 + RO$$

It is here when VOCs are involved with the ozone production, because atmospheric peroxides are formed in the oxidation processes of VOCs. In addition, tropospheric ozone concentrations are slightly affected also by the air streams from the stratosphere (Jacob, 2000). Destruction of ozone during daytime can occur by process involving sunlight:

$$O3 + h\upsilon \rightarrow O + O2$$
$$O_3 + O \rightarrow 2\ O_2$$

or more often during the night by catalytic reactions involving e.g. NO:

$$NO + O3 \rightarrow NO2 + O2$$
$$NO_2 + O \rightarrow NO + O_2$$

Even though ozone in the troposphere is an oxidative air pollutant, we must not forget that this gas in the stratosphere has a vital function in inhibiting ultraviolet radiation from reaching the surface of the Earth.

Nitrogen dioxide (NO_2) is formed mostly in combustion processes of mobile sources involving nitrogen from air and from fuels (Vovelle, 2000). Nitrogen dioxide is also piercing smelling gas, whose color at high concentrations is reddish brown. Nitrogen oxides (NO_x), including NO_2 and nitrogen monoxide (NO), are primary pollutants and they perform as precursor pollutants for particulate matter and ozone.

Carbon monoxide (CO) is an odorless and tasteless gas that is derived from incomplete burning of carbon-containing compounds. Carbon monoxide is formed instead of carbon dioxide when there is insufficient amount of oxygen available for the combustion process (Vovelle, 2000). Natural sources of CO are volcanic eruptions and bush and forest fires.

Sulfur dioxide (SO_2) is a by-product of burning of sulfur containing fuels. Sulfur content differs between fuels, coal and diesel having higher sulfur content than gasoline (Vovelle, 2000). Prior to the advancing of particulate matter measurements, SO_2 was often used as The air pollution measure in epidemiological health studies. However, as a result of SO_2 restrictions, the combustion processes have thereafter developed and the levels of SO_2 have declined to levels with minor health effects.

2.2 Health effects of ambient air pollution

2.2.1 General health effects of ambient air pollutants

The health effects of air pollutants were first observed after the massive smog episodes in the Meuse valley, Belgium in 1930, and in London in 1952. The described health effects considered associations between sulfur dioxide and cardiopulmonary health (Ministry of Health, 1954; Nemery et al., 2001). By the late 1970's the levels of air pollutants had remarkably decreased as a result of successful emission control efforts, and the common opinion was that no health effects at the prevailing levels would occur (Brunekreef and Holgate, 2002). However, in the early 1990's when two large cohort studies from North America revealed associations between mortality and air pollutants at moderately low levels (Dockery et al., 1993; Pope et al., 1995), a new era of air pollution research commenced.

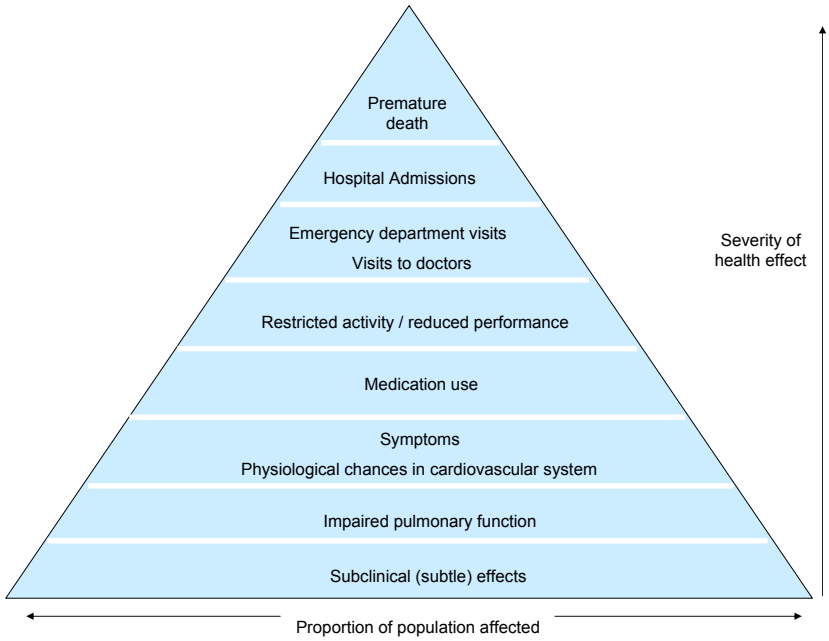
In numerous researches, associations for short-term and long-term exposure to particulate pollutants with various health outcomes have been observed. (Brunekreef and Holgate, 2002; Pope and Dockery, 2006). The acute effects have been studied by determining the effects of daily variation in air pollutant levels on daily morbidity or mortality counts. Morbidity, studied as increased hospital admission and emergency room visit counts, and as less severe outcomes like respiratory symptoms, and changes in vascular system, has been associated with exposure to air pollutants at short term (Brunekreef and Holgate, 2002; Delfino et al., 2005; Koenig, 1999). Short-term exposure to air pollutants has also shown to increase mortality (Mar et al., 2000; Samoli et al., 2008; Wichmann et al., 2000). Short-term studies, especially panel studies, have also been used to study the effect mechanisms of pollutants. In these studies outcomes such as inflammation markers and electrocardiography parameters have been studied (Gold et al., 2000; Ruckerl et al., 2007a). The effects of long-term exposure have been studied in cohort studies, where increased cancer mortality among other outcomes has also been linked to ambient air pollutants (Brunekreef, 2007; Chen et al., 2008; Dockery et al., 1993).

Some population groups have also been found to be more sensitive to the effects of ambient air pollution than others. Children and the elderly, people with cardiopulmonary diseases such as acute respiratory infections, congestive and ischemic heart disease, defects in the electrical control of the heart, hypertension, influenza, COPD, or asthma have shown to be particularly vulnerable to the effects of pollutants (Annesi-Maesano et al., 2003; Bateson and Schwartz, 2004; Berglind et al., 2008; Peel et al., 2007; Pope, 2000; Wellenius et al., 2005; Zanobetti et al., 2000). There are also suggestions that diabetics suffer from milder exposures to ambient pollutants than healthy individuals (Gold, 2008;

Goldberg et al., 2001c; Peel et al., 2007; Zanobetti and Schwartz, 2001). However, no matter how low the exposure to pollutants is, a threshold level under which harmful health effects would not occur has not been found (Schwartz et al., 2002).

The levels of the severity of the health effects, and proportion of population affected on each level is illustrated in Figure 1. It can be seen at the bottom of the pyramid that the population affected by less severe outcomes is much larger than population that suffers from the more severe outcomes such as mortality or hospitalization. This suggests that the effects observed in mortality studies are only the tip of the iceberg when considering the entity of health effects caused by air pollution (WHO, 2005).

The health effects of long-term and short-term exposure to air pollutants have been studied in cohort and time-series, which form the basis for the regulations of air pollutant levels (Bell et al., 2004b; U.S.EPA, 2006; WHO, 2005). Cohort studies are longitudinal studies used for estimating the effects of chronic exposure to pollutants, covering also partly the short-term effects. Ability to cover both long- and short-term exposure is the main strength of cohort studies. Time-series studies, on the other hand, estimate only the effects of short-term changes (usually daily) in air pollution on the short-term (daily) changes in a health outcome. Advantage of cohort and time-series studies is the large number of cases, which increases the power of the analyses, and also gives possibility to study rare diseases. Time-series studies have also low costs, because data collection from registers and air pollution monitoring are inexpensive. However, results from time-series studies are sometimes thought to underestimate the total effect size, which relates to the absence of estimation of long-term effects. This means that air pollution can increase the risk of chronic diseases leading to frailty but is unrelated to timing of death (Kunzli et al., 2001; Ren and Tong, 2008). Short-term studies have sometimes been criticized also because the findings are thought to be a result of "harvesting effect". This means that deaths or hospitalizations would increase among those persons who are the sickest and would have died or become hospitalized in few days anyhow (Rothman, 2002). It seems, however, that harvesting does not explain the observed acute effects (Schwartz, 2001), and therefore also results from time-series studies are valid to be used in the regulation processes.



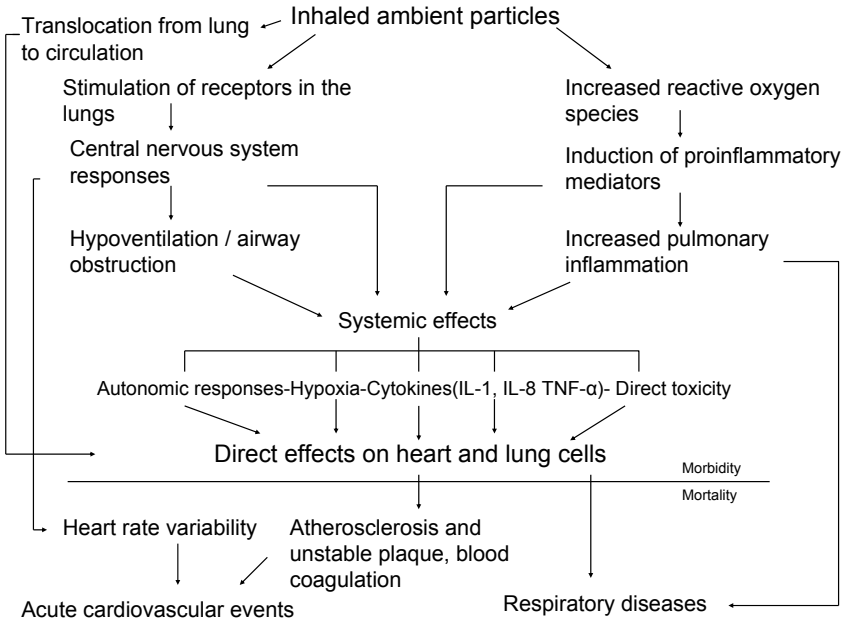
Source: (American Thoracic Society, 2000)

Figure 1. Pyramid of health effects associated with air pollution.

2.2.2 Possible mechanisms of ambient air pollutants on cardiorespiratory health

To better understand and avoid the harmful effects of air pollutants, the mechanisms of the health effects have been under vigorous investigation. For fine and ultrafine particles, the suggestive effect mechanisms are presented in Figure 2.

Particulate matter deposited in the airways can cause epithelial barrier disruption via oxidative and toxic compounds imported on their surface (Costa and Dreher, 1997; Gilmour et al., 1996; Vinzents et al., 2005). Structural changes in the mucosal membranes and disruption of the epithelial barrier caused by irritation can lead to pulmonary dysfunctions and increase the permeability of airway epithelia (Timonen et al., 2004). Increased permeability facilitates further the penetration of macromolecules and particulate matter into the epithelium tissue and circulation (Bhalla, 1999; Chuang et al., 2007).



Modified from: (Godleski et al., 2000)

Figure 2. Hypothetical mechanisms by which ambient fine and ultrafine particles end in morbidity and mortality.

Inflammation, a mechanism that lies behind several pulmonary and extra-pulmonary diseases, can be induced by the oxidative stress following particulate exposure (Brook et al., 2004; Delfino et al., 2005; Rahman and MacNee, 1998) (Figure 2). In pulmonary inflammation, cytokines such as interleukins 1 and 2 are released that further activate the defense mechanisms in the airways. Local inflammation may also lead to systemic inflammation where inflammation markers such as fibrinogen and C-reactive protein are released into the blood circulation. (Gabay and Kushner, 1999). Systemic inflammation in the airways leads to deterioration of lung function (Thyagarajan et al., 2006), and it possibly increases the risk of chronic pulmonary disease, cardiovascular disease and several neurological and skeletal defects (Agusti, 2005). The cardiovascular effects of particles may also occur through local inflammation in the blood vessels. Inflammation can induce the formation of plaques that may rupture as a result of sudden increase in blood pressure, for example. This can cause thrombus in the heart or brain vessels, which

are observed as myocardial infarction or ischemic stroke, respectively. Inflammation may also increase the levels of interleukin 6 that promotes blood clotting, which also increases the risk of cardiac arrest and stroke (Samet et al., 2007).

The effect of fine particles on cardiovascular system has also been suggested to occur via mechanisms including the autonomic nervous system. In the respiratory system several sensory receptors become activated by chemical components on inhaled particles, through oxidative stress, or through inflammation. This induces reflex changes in the cardiovascular system (Widdicombe and Lee, 2001). The autonomic nervous system controls heart rate variability (HRV) that thus can be affected by short-term exposure to air pollutants (Chuang et al., 2007; Gold et al., 2000; Lipsett et al., 2006; Timonen et al., 2006; Yeatts et al., 2007). Changes in HRV further increase the risk of myocardial ischemia and the risk of arrhythmias especially among susceptible persons (Berger et al., 2006; Rich et al., 2005). In addition, the autonomic nervous system, the current state of the myocardium, and myocardial vulnerability are contributing to the cardiac morbidity and mortality as presented by Zareba et al. (2001).

The effect mechanisms of ultrafine particles are partly the same as those of fine particles. However, it has been shown that ultrafine particles cause more oxidative stress than larger particles (Li et al., 2003). Reason for the greater oxidative capacity maybe the small size or large number of particles, because ultrafine particles composed also of non-toxic substances have been found to be harmful (Donaldson and Stone, 2003; Monteiller et al., 2007; Nel et al., 2006). Carbon black particles and aggregates of ultrafine particles can also impair the phagocytosis of human macrophage cell line to a greater extent than fine particles, which is why inflammation possibly occurs more readily after exposure to ultrafine particles compared to fine particles (Donaldson et al., 2001; Lundborg et al., 2006; Renwick et al., 2001). However, opposite results have also been found, showing higher inflammation marker occurrence after exposure to fine or coarse particles than ultrafine particles (Becker et al., 2005).

Another effect mechanism of ultrafine particles is suggested to be the translocation of particles into the circulation and further into secondary target organs (Nemmar et al., 2002; Nemmar et al., 2004; Oberdorster et al., 2005). However, it has been reported that only 5% of the deposited particles in the lungs is systemically translocated (Kreyling et al., 2006). Thus it can be that the effects of the smallest particles are due to their larger surface area that determines the potential number of reactive groups on particle surfaces, rather than the small size alone. Among the reactive groups on ultrafine particle surfaces are metals. Evidence of the toxicity of particle coating metals has been found in cell and animal studies, where iron, silicon, zinc, copper, manganese, nickel, and vanadium have been associated with increases in various inflammation markers (Becker et al., 2005; de Kok et al., 2006; Molinelli et al., 2006; Rice et al., 2001).

Health effects of coarse particles may also occur via the inflammatory cascade (Schins et al., 2004). Especially, the endotoxin contaminants of particles have been linked to the harmfulness of coarse particles (Becker et al., 2003; Huang et al., 2002; Schins et al., 2004). Besides endotoxins, the insoluble components of coarse particles can modulate the functionality of alveolar macrophages (Soukup and Becker, 2001). Coarse particles have also been found to activate monocytic cells, which may enhance responses to allergens or bacteria in individuals with allergy (Alexis et al., 2006). However, relatively little knowledge is available on the exact mechanisms of health effects of coarse particles.

Causality of the health effects of gaseous pollutants ozone and nitrogen dioxide derives from the oxidative capacity of these gases. However, direct contact between gases and pulmonary epithelial is unlikely, because O_3 and NO_2 react readily with substrates in the lung lining fluid (Kelly and Tetley, 1997). Therefore, the deleterious effects are actually caused by the oxidized species that arise from these interactions, and that further can initiate inflammation (Kelly, 2003). The reactions of NO_2 and O_3 in the airways can also lead to increased sensitivity for allergic responses to allergens such as pollens.

The postulated mechanism through which CO could cause health effects differs from O_3 and NO_2. Carbon monoxide is not oxidative, but it can bind into cardiac myoglobin that normally delivers oxygen to the heart muscle (McGrath, 2000). Thus massive exposure to CO may lead to hypoxia, which increases the risk of cardiac events especially among people with heart disease. However, as the ambient levels of CO are rather low, it may be that only the vulnerable individuals suffer from the health effects of CO, and the mechanism for these effects are not completely determined (Hester and Harrison, 1998).

2.3 Epidemiological evidence of the short-term health effects of ambient air pollution in time-series studies

2.3.1 Methodology of time-series studies

In environmental epidemiology, longitudinal study designs such as time-series studies are often used for the study of the acute health effects (Ren and Tong, 2008). In time-series studies, the associations between daily changes in air pollution levels and daily variation in a health outcome are determined (Goldberg et al., 2008). The health effects are estimated by using regression models where the concentration of air pollutant is included in the model lagged from 0 (current day) to several days. Because the health effects are investigated within the same geographical area, the population serves as its own control, and the confounding by population characteristics (occupation, socioeconomic status, smoking) is minor (Bell et al., 2004b). The same is true for other variables that are independent of time. However, some possible confounding factors, like weather, and time

dependent variables (weekday) that vary on day-to-day level must be considered in the regression models of time-series studies (Bell et al., 2004b).

The health data for time-series studies is often derived from health registers maintained by hospitals or other national institutions. This data usually includes cause-specific daily death, hospital admission, or emergency room visit counts by diagnoses for the population of the determined study area.

2.3.1.1 Air pollution measurements and possible measurement errors in time-series studies

Air pollution measurements for time-series studies are performed at one or several central measurement sites. Often the mass and number count concentrations are obtained from regular air quality monitoring networks. These pollutant levels are thought to be a proxy for average personal exposure, which, however, is not always the case. A problem with these measurements is that exposure assessment for the population in the study area varies, and also the exposure assessment for different particulate size fractions may vary. In the case of exposure within the population, bias may occur if the activity of an individual is correlated with the pollutant concentrations measured at central sites (Pekkanen and Kulmala, 2004). This is an example of so called Berkson error, which is suggested to cause little bias in epidemiological air pollution studies (Zeger et al., 2000). This is because error occurs only in the case when people respond to the possible weather and air pollution warnings by changing their daily activities e.g. by reducing exercise or by opening or closing their windows. Particles in different size fractions, for one, have different source locations and the behavior and aerodynamic properties of particles differ by size (Kulmala et al., 2004). This leads to local variations in the exposure to different particulate fractions. Additionally, if particles produced from indoor sources have similar compositions than ambient particles, they may be also a cause for exposure misclassification (Zeger et al., 2000).

Earlier studies have shown that central site measurements of fine particles are valid enough to be used in epidemiological time-series studies (Hoek et al., 2008; Monn, 2001; Pekkanen and Kulmala, 2004; Tsai et al., 2000b). This is partly due to the even distribution of fine particles, and accumulation mode particles, over large areas because of their low deposition rate (Seinfeld and Pandis, 2006).

Unfortunately, central site monitoring values of ultrafine particle counts and coarse particulate mass are probably less valid proxies to be used for the personal exposure assessment than measurements of fine particles (Pekkanen and Kulmala, 2004). There are two main reasons for this. One is that the spatial variation in the ultrafine particle counts and coarse particle mass can be great. Ultrafine particles are rapidly diluted and condensed into larger particles when emitted, and therefore the concentration diminishes rather fast as the

distance from the source increases (Zhu et al., 2002a; Zhu et al., 2002b). Coarse particles, on the other hand, are often stirred up by wind and thereafter rapidly deposited because of their larger mass, which also leads to differences in spatial distribution. Another reason for the difficulties in accurate exposure assessment is the poor penetration of ultrafine and coarse particles through the wall and window structures of buildings (Long et al., 2001; Schulz, 2000). This derives from the high Brownian motion of ultrafine particles, and the greater size of coarse particles. However, in a recent study the correlations between night-time ultrafine number counts indoors and at central site seemed to correlate fairly well (Hoek et al., 2008). This implies that indoor sources such as cooking partly explain why the 24-hour correlations between indoor and outdoor ultrafine particle measurements are low. Indoor sources may also have a greater impact on the personal exposure to particles during winter time when infiltration of particles is lower than during summer (Brown et al., 2008).

In addition to the air-tightness of buildings, the amount and quality of air filtration has great effect on the indoor concentrations of outdoor particles (Hanninen et al., 2005) affecting also personal exposure. Air filtration has been shown to decrease the indoor levels of ultrafine particles more efficiently than the levels of accumulation mode particles (Hussein et al., 2004a; Koponen, 2001). However, the filtration efficiency is dependent on the filter type in use. In addition, air exchange rate affects the indoor levels of outdoor particulates, indoor concentrations following the changes in outdoor levels more accurately when air exchange rates are high (Guo et al., 2008). Because the indoor sources affect the indoor concentrations and personal exposure, recent studies have suggested that particles from ambient and non-ambient origin should be separated when studying the personal exposure and health effects of particulate matter (Ebelt et al., 2005; Wallace and Williams, 2005).

Exposure assessment for gaseous pollutants O_3, NO_2, and CO has rarely been validated in time-series studies. Air filters attached to mechanical ventilation can remove approximately 10% of the outdoor originated O_3 (Hyttinen et al., 2006; Hyttinen et al., 2003), and the half life of ozone indoors is short, probably less than 20 minutes (Jakobi and Fabian, 1997). However, there is little information about what the actual infiltration rate of O_3 is, how fast it reacts with indoor surfaces, and what is the role of by-products formed in the reactions between ozone and surfaces or other gases (Weschler, 2000). These by-products may include irritating substances such as formaldehyde and some carboxylic acids. Secondary organic aerosols also result from ozone reactions. Thus some of the respiratory health effects of ozone could be due to the exposure to these by-products indoors (Weschler, 2004).

Nitrogen dioxide, CO, and also ultrafine particles are mainly emitted from vehicles, which is why the levels of these three pollutants are highly correlated. Therefore many

studies have suggested that NO_2 and CO would be more of surrogates of the exposure to the mixture of traffic-related pollutants, than causal pollutants themselves (Cyrys et al., 2003; Fusco et al., 2001; Ruckerl et al., 2006). The spatial variation in NO_2 levels has been found to be greater than that of fine particles, but NO_2 is more stable in the atmosphere than ultrafine particles (Lewne et al., 2004). Thus NO_2 might particularly be a good surrogate for the exposure to traffic-related pollutants. Overall, the central cite measurements of fine particulate pollutants are considered as better surrogates of personal exposure than measurements of gaseous pollutants (Sarnat et al., 2006).

An alternative way to assess exposure to ambient air pollutants is modeling. However, when modeling the exposure, measurement errors may not be efficiently adjusted, and therefore exposure misclassification cannot be wholly avoided (Ren and Tong, 2008).

2.3.2 Effects of PM_{10}, $PM_{2.5}$ and gaseous pollutants

The short-term health effects of ambient air pollutants have been widely described in the literature. The two largest multi-city studies examining the short-term health effects of air pollutants so far have been the European study APHEA, and NMMAPS in the United States (Katsouyanni et al., 1996; Samet et al., 2000). Following these two time-series studies, a similar study in Asia (PAPA study: Public Health and Air Pollution in Asia) is ongoing (HEI, 2008; Wong et al., 2008). APHEA and NMMAPS studies also emerged as an ongoing project "Air Pollution and Health: A European and North American Approach" (The European Commission, 2002).

Several publications from APHEA and NMMAPS projects reported positive associations between various air pollutants and total mortality. In APHEA, 0.40% increase in total mortality in association with 10 $\mu g/m^3$ change in PM_{10} was found (Katsouyanni et al., 1997). In NMMAPS, the corresponding increase in mortality was 0.27%, pooled over 90 U.S cities (Dominici et al., 2005).

Of the gaseous pollutants, CO and NO_2 increased total mortality in the APHEA study (Samoli et al., 2006; Samoli et al., 2007). In NMMAPS the effect estimates for CO and NO_2 were positive though non-significant with one day delay (Dominici et al., 2005). However, ozone was linked with total mortality in both studies with 0.46% and 0.26% increase in total mortality (for 10 $\mu g/m^3$ increase in ozone) in Europe and USA, respectively (Bell et al., 2004a; Touloumi et al., 1997). Elevated ozone levels have been found detrimental especially for the respiratory system also in several other studies (Anderson et al., 1997; Medina-Ramon et al., 2006; Spix et al., 1998; Yang et al., 2003). However, the effects of ozone should be interpreted with some caution because exposure assessment for ozone is difficult. No studies have determined the indoor-outdoor ratio of ambient ozone concentrations, and because ozone reacts readily with any surrounding surfaces, the indoor

concentrations can be remarkably lower than those measured outdoors.

Since these two multi-city projects, air pollutant research has focused more on the smaller particles than PM_{10}, especially on $PM_{2.5}$. A 10 µg/m^3 increase in $PM_{2.5}$ has been estimated to cause approximately 1% increase in cardiovascular mortality (Pope and Dockery, 2006). Findings of the time-series studies estimating the effects of $PM_{2.5}$ and some other particulate measure on cardiovascular outcomes are listed in Table 1. Most studies found positive associations for fine and inhalable particles with cardiovascular mortality or morbidity. In about half of the studies, there were differences between particle fractions. In the other half of the studies presented in Table 1, the effect estimates were mostly comparable between different particle fractions.

Table 1. A summary of population level time-series studies estimating the health effects of more than one particulate fraction on cardiovascular health. Results are for one-pollutant analyses, covering the whole study period not restricted to seasons.

Particle size in µm	Age (if not all)	Effect estimate for 10 µg/m^3 increase in PM_{10}, $PM_{2.5}$ or $PM_{10-2.5}$	Lag	Reference
All Cardiovascular Mortality				
<2.5		1.3 (–0.9–3.5) †	1	(Lippmann et al., 2000)
2.5–10		3.1 (0.0–6.2)		
<10		1.3 (–0.3–3.0)		
<2.5		1.17 (1.12–1.32)	1	(Tsai et al., 2000a)
<15		1.11 (0.91–1.30)		
<0.1		0.45 (0.01–0.89)/1000	0–5	(Wichmann et al., 2000)
<2.5		2.53 (0.22–4.89) *	0–4	
<2.5	> 65	7.1 (2.4–12) *	1	(Mar et al., 2000)
<10		1.6 (0.02–3.2)		
<2.5		2.7 (0.9–4.5) *	0	(Ostro et al., 2000)
2.5–10		4.0 (0.9–7.1) *		
<10		7.6 (–5.6–22.5)		
<2.5		1.55 (–1.25–4.35)	5-d mean	(Castillejos et al., 2000)
2.5–10		4.54 (1.55–7.52)		
<10		2.00 (0.39–3.60)		
<2.5		1.3 (–0.5–3.2) †	1	(Goldberg et al., 2001b)
<10		0.9 (–0.3–2.1)		
<2.5		0.5 (–1.2–2.3) †	0-1-d mean	(Anderson et al., 2001)
<10		0.4 (–0.79–1.63)		
<2.5		1.7 (–6.7–10.9)	3–d mean	(Villeneuve et al., 2003)
<10		2.2 (–1.7–6.2)		
<2.5		0.41 (0.01 − 0.82)	0–1	(Kan et al., 2007)
2.5–20		0.34 (–0.05 − 0.73)		
<10		0.31 (0.10 − 0.53)		
Circulatory Mortality				
<2.5		2.9 (–4.2–10.5) *	1	(Ito, 2003)
<10		2.9 (–1.4–7.3)		

Table 1. continued

Particle size in µm	Age (if not all)	Effect estimate for 10 µg/m^3 increase in PM_{10}, $PM_{2.5}$ or $PM_{10-2.5}$	Lag	Reference
All Cardiovascular Admissions				
<2.5		–0.25 (–1.3–0.79) †	0-1-d mean	(Anderson et al., 2001)
<10		–0.22 (–0.94–0.50)		
<2.5		3.3 (1.1– 5.6) *	3-d mean	(Metzger et al., 2004)
<10		0.9 (–0.2–2.1)		
<2.5		1.0 (–3.0–5.2) *	3	(Slaughter et al., 2005)
<10		2.0 (–1.03–5.1)		
<2.5	≥ 65	6.10 (1.0–11.4)	0-3-d mean	(Andersen et al., 2007a)
<10		2.3 (0.8–3.9)		
<2.5		0.9 (0.1–1.8)	0-1-d mean	(Host et al., 2008)
2.5–10		0.5 (–1.2–2.3)		
<2.5		0.71 (0.45–0.96)	0	(Peng et al., 2008)
2.5–10		0.36 (0.05–0.68)		
Ischemic Heart Disease Admissions				
<2.5	≥ 65	–0.15 (–2.3–2.1) †	0-1-d mean	(Anderson et al., 2001)
<10		0.78 (–0.73–2.3)		
<2.5	≥ 65	4.8 (–2.7–12.9) *	2	(Ito, 2003)
<10		4.2 (–0.2–8.8)		
<2.5		2.3 (–0.2–4.8) *	3-d mean	(Metzger et al., 2004)
<10		1.1 (–0.9–3.1		
Heart Failure Admissions				
<2.5		5.5 (0.6–10.6) *	3-d mean	(Metzger et al., 2004)
<10		–0.8 (–3.2–1.7)		
<2.5	≥ 65	10.6 (1.8–20.1) *	1	(Ito, 2003)
<10		4.9 (–0.2–10.1)	0	
Dysrhythmia Admissions				
<2.5		1.5 (–2.4–5.6) *	0-2d mean	(Metzger et al., 2004)
<10		0.8 (–1.1–2.8)		
Peripheral Vascular Disease Admissions				
<2.5		5.0 (0.8–9.4) *	0-2d mean	(Metzger et al., 2004)
<10		2.0 (–0.1–4.2)		
Stroke				
<2.5	≥ 65	–0.8 (–3.4–1.8) †	0-1d mean	(Anderson et al., 2001)
<10		–1.24 (–3.0–0.55)		

* Percent change / 10 µg m^{-3} increase in particle measure calculated from originally given effect estimate of RR

† Original percent change calculated for other volume than 10 µg m^{-3} (e.g. % / 14.6 µg m^{-3}, or 36 µg m^{-3})

The effects of ambient air pollutants on respiratory health have generally been greater than the effects on cardiovascular diseases. One meta-analysis estimate presented in the literature suggests 1.3% increase in respiratory mortality for 10 µg m^{-3} increase PM_{10} (Anderson, 2004) compared to 1% increase in cardiovascular mortality (Pope and Dockery, 2006). The summary table of the time-series studies on respiratory outcomes shows that the sizes of the effect estimates between different particulate fractions have little variation (Table 2). On one hand, in five cases (Andersen et al., 2007a; Chen et al., 2004; Goldberg

et al., 2001a; Ito, 2003; Kan et al., 2007) the association for respiratory outcomes was found to be larger with $PM_{2.5}$ than with PM_{10} or coarse particles. On the other hand, in five other cases the association with PM_{10} or coarse particles was stronger compared to that with $PM_{2.5}$ (Andersen et al., 2007a; Atkinson et al., 2001; Castillejos et al., 2000; Peel et al., 2005).

Table 2. A summary of population level time-series studies estimating health effects of more than one particulate fraction on respiratory health. Results are for one-pollutant analyses, covering the whole study period not restricted to seasons.

Particle size in µm	Age (if not all)	Effect estimate for 10 µg/m³ increase in PM_{10}, $PM_{2.5}$, $PM_{10-2.5}$ or for 30 000/cm³ in UFP[a]	Lag	Reference
All Respiratory Mortality				
<2.5		3.6 (–1.06–8.27)	5-d mean	(Castillejos et al.,
2.5–10		8.03 (3.05–13.01)		2000)
<10		3.85 (1.16–6.55)		
<2.5		0.9 (–4.3–6.4) †	0	(Lippmann et al.,
2.5–10		2.9 (–3.7–10.0)	2	2000)
<10		1.5 (–2.1–5.3)	0	
<2.5		1.8 (0.6–3.1) *	0	(Wichmann et al.,
<0.1		1.11 (0.42–1.80)		2000)
<2.5		–0.9 (–5.4–3.8) *	0	(Ostro et al., 2000)
2.5–10		–1.9 (–9.5–6.3)		
<10		–11.8 (– 39–28)		
<2.5	≥ 65	5.1 (0.8–9.5) †	1	(Goldberg et al.,
<10		1.4 (–1.4–4.3)		2001b)
<2.5		–0.06 (–3.1–3.1) †	0-1-d mean	(Anderson et al.,
<10		–0.58 (–2.52–1.41)		2001)
<2.5		3.0 (–13–22) *	0	(Ito, 2003)
<10		4.0 (–5.8–14)		
<2.5		–0.8 (14.4–15.0)	3-d mean	(Villeneuve et al.,
<10		0.0 (–6.2–6.7)		2003)
<0.1		16 (–5.3–43) †*	0	(Stolzel et al.,
<2.5				2007)
<2.5		0.95 (0.16–1.73)	0–1	(Kan et al., 2007)
2.5–10		0.40 (–0.34–1.13)		
<10		0.33 (–0.08–0.75)		
All Respiratory Admissions				
<2.5	0–14	1.7 (–0.05–3.5) †	0-1-d mean	(Anderson et al.,
<10		1.4 (–0.2–2.7)		2001)
<2.5	15–64	–1.1 (–3.3–1.2) †	0-1-d mean	(Anderson et al.,
<10		0.04 (–1.5–1.6)		2001)
<2.5	≥ 65	–0.7 (–2.4–1.1) †	0-1-d mean	(Anderson et al.,
<10		–0.4 (–1.6–0.8)		2001)
<2.5		1.0 (–2.0–4.1) *	3	(Slaughter et al.,
<10		1.0 (–2.7–4.8)		2005)
<2.5	≥ 65	0.8 (–2.8–4.5) *	0	(Fung et al., 2006)
<10		2.0 (–0.2–4.3)		
<2.5	≥ 65	0.0 (–9.8–10.8) *	0-4-d mean	(Andersen et al.,
<10		3.7 (1.6–5.9)		2008)

Table 2. continued

Particle size in µm	Age (if not all)	Effect estimate for 10 µg/m³ increase in PM_{10}, $PM_{2.5}$, $PM_{10-2.5}$ or for 30 000/cm³ in UFP[a]	Lag	Reference
<2.5	≥ 65	0.5 (–2.0–3.0)	0-1-d mean	(Host et al., 2008)
2.5–10		1.9 (–1.9–5.9)		
<2.5		0.44 (0.06–0.82)	0	(Peng et al., 2008)
2.5–10		0.33 (–0.21–0.86)	2	
Asthma Admissions				
<2.5	≤18	2.4 (1.4–3.5) †	4	(Lee et al., 2006)
<10		2.2 (1.6–2.7)		
<0.1		–0.09 (–2.2–2.1)	0-2-d mean	(Peel et al., 2005)
<2.5		0.5 (–2.2–3.3)		
<2.5	5–18	32 (0.0–75) *	0-5-d mean	(Andersen et al.,
<10		4.0 (–13.5–25.1)		2008)
<2.5		0.9 (0.4–1.4)	0-1-d mean	(Ko et al., 2007)
<10		0.8 (0.4–1.2)		
Asthma–COPD Admissions				
<2.5		2.0 (–7.0–12) *	3	(Slaughter et al.,
<10		1.0 (–7.9–10.7)		2005)
COPD Admissions				
<0.1		–1.8 (–5.8–2.3)	0-2-d mean	(Peel et al., 2005)
<2.5		1.5 (–3.1–6.3)		
<2.5	≥ 65	3.9 (–8.9–18.6) *	3	(Ito, 2003)
<10		3.4 (–4.3–11.7)		
<2.5	≥ 65	17 (4.6–31) *	0	(Chen et al., 2004)
<10		10.9 (3.8–18.5)		
<2.5	adults	6.0 (–2.5–15.3) *	2	(Slaughter et al.,
<10		3.0 (–4.1–10.6)		2005)
Pneumonia Admissions				
<2.5	≥ 65	13 (2.5–26.6) *	1	(Ito, 2003)
<10		9.4 (2.8–16.3)		
<0.1		–2.2 (–4.7–0.2)	0-2-d mean	(Peel et al., 2005)
<2.5		1.1 (–1.9–4.2)		

[a] ultrafine particles, <0.1µm

* Percent change / 10 µg m^{-3} increase in particulate measure calculated from originally given effect estimate of RR

† Original percent change calculated for other volume than 10 µg m^{-3} (e.g. % /14.6 µg m^{-3}, or 36 µg m^{-3})

2.3.3 Effects of ultrafine and coarse particles

Besides PM_{10} and $PM_{2.5}$, ultrafine particles have caught the interest of researches. In the first time-series studies using measured data on ultrafine particles, positive associations between ultrafine particles and all respiratory and asthma morbidity have been reported (Andersen et al., 2008; Peel et al., 2005). In both of these studies the associations with ultrafine particles were more than 2-days lagged. Similar effect lag structure was reported also in a German study on the effects of ultrafine particles on mortality (Breitner et al., 2009; Stolzel et al., 2007; Wichmann et al., 2000). On the other hand, results of the multi-city study HEAPSS, suggested more rapid effect of ambient particle number count on the

risk of first acute myocardial infarction and cardiac readmissions (Lanki et al., 2006b; von Klot et al., 2005), and in a case-crossover study in Italy, out-of-hospital coronary deaths were associated with the current-day levels of particle number count (a proxy for ultrafine particles) (Forastiere et al., 2005). However, only a few epidemiological time-series studies, much less cohort studies, so far have been able to determine the health effects of ultrafine particles. Therefore, the current epidemiological evidence of the health effects of ultrafine particles still relies more on the results of panel studies that have been carried out among susceptible population groups.

In panels among asthmatics, associations between ultrafine particles and respiratory health decrements have been reported in Finland and elsewhere (Ibald-Mulli et al., 2002; McCreanor et al., 2007; Penttinen et al., 2001a, b). In the ULTRA study, a decrease in LF/HF ratio in association with ultrafine particles suggested that air pollution may lead to increased cardial vagal control (Timonen et al., 2006). In addition, in Germany ultrafine particles, among other air pollutants, have been linked to inflammatory responses among patients with coronary heart disease (Ruckerl et al., 2006; Ruckerl et al., 2007b). However, extrapolation of the result of panel studies to general population is not straightforward. In few experimental studies, healthy young people have been exposed to concentrated levels of ultrafine particles, and mild inflammatory and pro-thrombic responses have been observed also suggesting adverse effects caused by ultrafine particles (Samet et al., 2007; Samet et al., 2009). However, more research on the health effects of ultrafine particles on population level is needed.

Health effects of coarse particles have been studied more often in time-series studies than the effects of ultrafine particles. In the U.S Six Cities Study, a 0.4% (95% CI -0.1–1.0) increase in total mortality (for 10 $\mu g/m^3$ coarse PM) was found (Klemm et al., 2000; Schwartz et al., 1996). Similarly, Peng et al. (2008) recently reported a 0.36% (95% posterior interval, 0.05%–0.68%) increase in cardiovascular disease admissions for 10 $\mu g/m^3$ increase in coarse particle concentration on the same day. However, this association was sensitive to adjusting for $PM_{2.5}$ and the association between cardiovascular admissions and $PM_{2.5}$ was greater than that of coarse particles. Positive association between coarse particles and respiratory hospitalizations among the elderly has also been reported in a Canadian study (3.96%, 95% CI 0.70–7.33, for 10 $\mu m/m^3$) (Fung et al., 2006), and coarse particles have been found to affect heart rate variability and lipid parameters among asthmatic adults in North Carolina (Yeatts et al., 2007). The conclusion of the latest review on coarse particles by Brunekreef and Forsberg (2005) was that there is evidence of the health effects of coarse particles, but more research is still needed.

2.3.4 Effects of ambient particles from different sources

As the harmful effects of ambient particles on health have been found in many epidemiological studies (Tables 1 and 2), the limit and target levels have already been set for PM_{10} and $PM_{2.5}$ (European Union, 2005; WHO, 2005). However, to be able to control for the most harmful particle emissions, the question of what sources emit the most harmful particles has to be thoroughly studied.

Few epidemiological health studies have had data for the apportionment of various sources of measured ambient particles. There is some evidence showing that the effects of various $PM_{2.5}$ components on health are different from each other. Most often, the harmful effects have been associated to traffic and combustion derived particles (Table 3). Recently, for example, Sarnat et al. (2008) apportioned ambient $PM_{2.5}$, and found that admissions for cardiovascular outcomes increased in association with $PM_{2.5}$ from automobiles and biomass burning. They reported also associations between sulfate-rich secondary $PM_{2.5}$ and respiratory morbidity. Local combustion particles and exposure to traffic have been linked to the decrease in lung function among asthmatics (McCreanor et al., 2007; Penttinen et al., 2006), and total and cardiovascular mortality have also been linked to traffic-related $PM_{2.5}$ in several studies in the United States (Laden et al., 2000; Mar et al., 2000; Ostro et al., 2007). In two of these studies also $PM_{2.5}$ from coal and biomass combustion affected mortality rates (Mar et al., 2000; Ostro et al., 2007). Traffic related particles seem to associate with the health outcomes in most studies presented in Table 3, whereas the effects of sea salt particles seem weaker.

Table 3. Studies that have determined the short-term health effects of source apportioned ambient particles. + indicates a positive finding between the particle source and a health outcome, - indicates that no health effects were observed, empty square indicates that the particle source was not identified.

Author	*Outcome*	*PM Source*						
		Traffic	Soil / Crustal	Oil combustion	Biomass combustion	LRT / Secondary sulphate	Sea Salt	Other
Time-series studies								
Mar [a] (2000)	Cardiovascular mortality	+	-		+	+		
Laden [a] (2000)	Total mortality	+	-				-	Coal combustion
Tsai [a] (2000a)	Total mortality	+	- [c]	+		+		Industrial
Janssen [b] (2002)	Cardiovascular admissions	+		+	-			Metal processing
	Pneumonia admissions	+		-	-			-
Andersen [b] (2007a)	Cardiovascular admissions	-	+	+	+	+	+	
	Respiratory admissions	-	+	+	+	+	+	
	Asthma admissions	+	-	-	-	-	-	
	Cardiorespiratory mortality	-	-	+		+		
Sarnat [a] (2008)	Respiratory visits	-	-		-	+		
Panel studies								
Lanki [a] (2006a)	ST segment depression	+	-	-		+	-	
Penttinen [a] (2006)	PEF deviation	+	-	-		-	-	
Yue [a] (2007)	Inflammatory marker C-reactive protein	+	+			+		
	Re-polarization parameter	+	-			-		
	Cardiovascular disease visits	+	-		+	-		Organic carbon
De Hartog [a] (2009)	Heart rate variability	+	-	-		+	-	

[a] apportioned particulate measure was $PM_{2.5}$, [b] apportioned particulate measure was PM_{10}, [c] Geological source

2.3.5 Effects of pollutants in different age groups

Susceptibility to the effects of air pollutants among people at different ages has been hypothesized to differ. Most often children and the elderly are considered as the most sensitive population groups (Anderson et al., 2003; Goldberg et al., 2001c; Schwartz, 2004). Even unborn children have been found to be at risk of the effects of pollutants when their mothers are exposed to air pollutants (Pereira et al., 1998; Salvi, 2007). In children, the defense mechanisms against xenobiotics are immature and therefore the ability to metabolize, detoxicify, and excrete environmental agents is lower than in adults (Kajekar, 2007). The exposure to air pollutants is also higher among children because they have higher ventilation rates than adults, they are more active, spent more time outdoors, and they breath at the height of the traffic emission sources (Heinrich and Slama, 2007; Klepeis et al., 2001; Schwartz, 2004; Wigle et al., 2007). Another reason for the vulnerability may be that children tend to be mouth-, rather than nasal-, breathers, which suggests that pollutants reach lower parts of the lung, and that the composition of pollutants at alveolar level may be different from that of adults (Bateson and Schwartz, 2008).

The elderly, on the other hand, often have underlying diseases that make them more vulnerable to the effects of air pollutants than adults (Anderson et al., 2003; Bateson and Schwartz, 2004; Peel et al., 2007). Aging causes biological changes in the body such as reductions in lung or cardiac function, and reduced resistance to infections. In addition, poor diet may occur more often among the elderly and that may also reduce the defense mechanisms against air pollutants. This is because the lack of antioxidants of dietary origin may reduce the protective mechanisms of the respiratory tract lining fluid that becomes first affected by inhaled air pollutants (Kelly et al., 2003). Exceeding the critical threshold of the health effects may thus occur after milder exposure to air pollution compared to individuals whose antioxidant intake is sufficient. At the same time, however, elderly people have been exposed to air pollutants during a longer time period, which may also cause chronic health effects (Anderson et al., 2003).

2.4 Ambient air pollution studies in Finland

In Finland, the linkage between air pollution data and health effects has been studied since the late 1980's when interest in the effects of low to moderate air pollution levels was aroused. Air pollution health studies have been possible due to the national health care system with high coverage, and extensive health, air pollutant, and meteorological data (Ponka, 1995). The earliest time-series studies in Finland were mainly performed by researchers Pönkä and Virtanen in Helsinki. Later, several researches have been performed with measurements from either Helsinki or Kuopio. These two cities have been

the companion cities in European multi-city projects such as PEACE, HEAPSS, APHEA (1 and 2), ULTRA and AIRGENE.

2.4.1 Population level time-series studies

Before investigations focused on the Helsinki metropolitan area, a study between air pollution and asthma emergency room visits was performed in Oulu (Rossi et al., 1993). In this study, authors found an association between asthma visits and ambient NO_2, however, the data included measurements for only one year. The first population level time-series studies from Helsinki region included data for three years (1987–1989). These investigations revealed various associations between air pollutants and hospital admissions in the total population. Respiratory admissions were found to be associated with increases in SO_2, NO_2, and O_3 at selected lags (Ponka and Virtanen, 1994, 1996a), and cardiovascular admissions seemed to be associated with NO (Ponka and Virtanen, 1996b). First time-series studies on mortality had data over a longer time period from 1987 to 1993. Cardiovascular mortality among people less than 65 years was linked to increases in PM_{10}, O_3, and NO_2 (Ponka et al., 1998), and some years later (data for 1988–1996), respiratory mortality in the total population was also linked to increased PM_{10} and O_3 levels (Penttinen et al., 2004).

However, the previous studies (Ponka and Virtanen, 1994, 1996a, b; Rossi et al., 1993) have had access to a limited number of measurement days and air pollution measures, and the health effects of ambient particles from different sources in Finland have not been determined in earlier time-series analyses.

Helsinki was one of the participating cities in the APHEA (1985–1990) and APHEA II (1991–1996) projects where time-series method was used. Asthma hospital admissions of adults were found to be associated with the levels of gaseous pollutants SO_2, NO_2, and O_3 in Helsinki (Sunyer et al., 1997). Positive associations of CO and NO_2 with total and cardiovascular mortality were also reported, but in the city-specific analyses the associations in Helsinki were negative (Samoli et al., 2006; Samoli et al., 2007). Similarly, the association between cardiovascular mortality and PM_{10} in Helsinki was negative (Analitis et al., 2006). In agreement with previous results of Penttinen and co-workers (2004), respiratory mortality had a positive association with PM_{10} levels also in Helsinki (Analitis et al., 2006).

In the HEAPSS study, daily variation in hospital admissions for acute myocardial infarction (MI) in Helsinki (1993–1999) was investigated. Here, Lanki et al. (2006a) found that particle number count, a proxy for ultrafine particles, and CO were associated with an increase in MI admissions. Pooled relative risks for all five cities, and for Helsinki only were 1.005, 95% CI 0.996–1.015, and 1.041, 95% CI 0.970–1.117, respectively,

for 10 000 1/cm^3 increase in particle number count. In this study, however, the particle number count measurements were performed only for one year and the rest of the data was modeled**.** In a cohort of myocardial infarction survivors in the HEAPSS study, an increased risk of hospital cardiac readmissions was observed in association with PM_{10} in Helsinki (von Klot et al., 2005).

2.4.2 Panel studies

More often than time-series studies, panel studies on the health effects of air pollutants have been carried out in Finland. The Finnish participant city in the PEACE study was Kuopio. The measurements for the panel of asthmatic children were carried out during winter 1993–1994. The main finding was that morning peak expiratory flow (PEF) was reduced in association with increase in PM_{10}, TSP and NO_2 with two days delay (Pekkanen et al., 1997; Timonen and Pekkanen, 1997). The participants of the PEACE study were included also in another panel that investigated the effects of particulate pollutants on PEF and respiratory symptoms (Tiittanen et al., 1999). In this study, some evidence of the associations between different ambient particulate size fractions and respiratory symptoms were observed.

Personal exposure to and the health effects of weekly averages of NO_2 were studied among a panel of preschool children in Helsinki in 1990–1991. Respiratory symptoms were found to be associated with low levels of NO_2 (Mukala et al., 1999). In a later panel study, in 1996–1997, asthmatic adults in Helsinki were investigated. Ultrafine and accumulation mode particles were associated with PEF and spirometric lung function decrements on the same and previous day (Penttinen et al., 2001a, b). These results suggested that traffic-related pollutants (NO_2 and ultrafine particles) exacerbate respiratory symptoms especially among asthmatics. Later on, analyses on the effects of fine particle sources on morning PEF among adult asthmatics led to a similar conclusion; $PM_{2.5}$ from local combustion processes such as traffic, and from long-range transport were mainly responsible for the observed respiratory health effects (Penttinen et al., 2006).

The international ULTRA study examined a panel of subjects with coronary heart disease during winter 1998–1999. Here, Pekkanen et al. (2002) found that ST-segment depression during exercise was associated with an increase in particles in the ultrafine and fine size fraction two days prior the test, which suggests that cardiovascular effects of particles can be partly due to myocardial ischemia. Other reported findings of the UTLRA study were a 2-day lagged association between ultrafine particles and Clara cell protein CC16, a marker of lung damage (Timonen et al., 2004), the association between shortness of breath and increases in $PM_{2.5}$ levels at lags 0 to 3 days in Helsinki (de Hartog et al., 2003), and a 0 to 2 days lagged association between heart rate variability and ultrafine and

fine particle levels (Timonen et al., 2006). Short-term, even hourly changes in the personal and outdoor $PM_{2.5}$ levels were also associated with ST-segment depressions (Lanki et al., 2008), and 2 to 3-days lagged associations were reported between outdoor $PM_{2.5}$ and decreased heart rate variability (de Hartog et al., 2009). The ULTRA study also tried to determine the most harmful particle sources. Similarly to the studies by Penttinen et al. (2006), and by Lanki et al. (2006b), the authors suggested that particles from combustion processes, mainly from local traffic, but also particles from long-range transport are the most harmful for health (de Hartog et al., 2009; Lanki et al., 2006a).

In the AIRGENE study associations between ambient air pollutants and inflammation markers were studied in six European cities. In the pooled analysis for the six cities, exposure to particle number count 12–17 hours prior the test increased IL-6 levels in blood (Ruckerl et al., 2007a). However, in Helsinki, a positive association was observed only for the change in blood fibrinogen level with particle number count and PM_{10} concentration.

As described above, several associations have been found between air pollutants and health outcomes in panel studies in Finland. However, there are few limitations in panel studies, which is why also population level studies are needed. One is that the results can rarely be generalized across the total population, because panels are assembled of people with a specified underlying illness, who therefore are at higher risk to respond to air pollution exposure to begin with. Moreover, the outcomes studied in panel studies are usually sub-clinical changes, which means they are not as severe as hospitalizations or mortality that can be the outcomes in time-series and cohort studies. The study of rare diseases is neither possible in a panel, and often the low number of cases reduces the statistical power of the analyses (Lagorio et al., 2006). Benefits of panel studies include the possibility to study the mechanism that mediates the effects of air pollution. Repeated measurements can provide better power for the study and better adjustment for unknown confounders. More accurate personal exposure assessment is also possible in panel studies compared to time-series studies. However, this greatly increases the costs of the studies. In addition, the measurement periods in panel studies do not usually cover the whole year. Since particle mass compositions vary between seasons, because the particle source contributions are not the same through the year, the results may not be applicable to other seasons than that under investigation.

2.4.3 Characteristics of air pollutants in Helsinki

Helsinki metropolitan area is located in the Northern hemisphere by the Gulf of Finland. The location induces some characteristics to the air pollution levels in the area as wind from the sea dilutes the local emissions. Because of the marginal location, air pollutant levels, except for ozone, in Helsinki are generally low compared to big Central European,

North American or Asian metropolises.

The prevailing south-western winds transport more than half of the total $PM_{2.5}$ mass measured in Helsinki from Central European and Baltic countries, and from Russia (Kulmala, 2000; Vallius et al., 2003). The other half of particulate matter is derived from local sources and mainly from traffic, but also from coal and oil combustion processes, wood combustion, wearing of soil and roads, re-suspension of road dust, and from sea salt. The air quality guideline by WHO determines that the annual level of $PM_{2.5}$ should be below 10 $\mu g\ m^{-3}$ (WHO, 2005) – this is reached well in Helsinki with an average level of $PM_{2.5}$ around 9 $\mu g\ m^{-3}$.

The 24-hour average levels of inhalable particles, PM_{10}, in Helsinki exceed the guideline level of 20 $\mu g/m^3$ set by WHO (WHO, 2005) every year. This is because of the road dust episodes that occur at spring time. The dust derives from traction sanding that is necessary for the prevention of slipperiness of roads during winter, and also from the use of studded tires that leads to increased levels of asphalt aggregates (Kupiainen et al., 2005). Other reasons for particulate matter episodes in Helsinki are particles from open biomass burning e.g. forest fires in Eastern Europe (Niemi et al., 2009).

Ultrafine particle levels in Helsinki, on the other hand, are similar to the levels in other big cities in Northern and Central Europe (Ruuskanen et al., 2001). This is because the sources of ultrafine particles are local and they are not affected by particles transported from elsewhere. Like anywhere, local combustion processes such as traffic are the main source of ultrafine particles in Helsinki.

Like fine particles, ozone can be transported over long distances as it has been found to be associated to SO_4^{2-} that is an indicator of long-range transport and secondary particles (Sarnat et al., 2001). Therefore long-range transportation from Central Europe affects also ambient ozone levels in Southern Finland (Laurila, 1999). The highest ozone levels are measured during the spring and summer time, when the temperature is favorable, and amount of sunlight is adequate for local ozone formation. At the same time, transportation of O_3 during high pressure weather conditions can be intense. Guidelines for the ozone levels have also been determined by WHO (WHO, 2005). In Helsinki, the limit level for the maximum 8-hour moving average (100 $\mu g\ m^{-3}$) is exceeded few times every year, most often during March or April.

The other gaseous pollutants, NO_2 and CO, are mainly derived from traffic emissions in Helsinki, and the levels of these gases are generally below the limit levels. For example, in 2005, the level of NO_2 exceeded the daily guideline level (70 $\mu g\ m^{-3}$) only few times in the very vicinity of busy roads in the city center. The exceeding of the limit value may have occurred because of inversion situations during winter time when pollutants cannot be mixed to larger air masses. However, the hourly NO_2 values were constantly well below the maximum hourly guideline value (200 $\mu g\ m^{-3}$) set by WHO. The levels of CO

in Helsinki are also frequently less than one tenth of the limit value (10 mg m^{-3}, maximum 8-hour moving average), set by the European Community.

3 AIMS OF THE STUDY

Continuous measurements of different ambient particle size fractions began in 1997 in Helsinki. Together with regular monitoring data of other air pollutants there was an extensive database of air pollutant levels for a time-series analysis. Register-based health data over 7 years provided also high enough number of morbidity and mortality cases to attain statistical power for the analyses, and enough cases also for cause- and age-specified analyses.

The aims of this study were to determine

1) Are there differences between the short-term effects of air pollutants on cause-specific cardiovascular and respiratory health in Helsinki metropolitan area?
2) Which of the particle size fractions and $PM_{2.5}$ sources are the most harmful for human health?
3) Are there differences in the vulnerability to air pollutants between different age groups?

4 MATERIALS AND METHODS

4.1 Study area, mortality and morbidity data

The study measurements took place in the metropolitan area of Helsinki that consists of four municipalities: Helsinki, Vantaa, Espoo, and Kauniainen (one million inhabitants, 745 km^2) in 1998–2004.

We obtained the daily mortality data from Statistics Finland, and acute hospital admission and emergency room visit data from National Research and Development Center for Welfare and Health (currently National Institute of Health and Welfare). Hospital admissions were collected from the hospital discharge registers from all hospitals in the study area, and only those cases when patient had stayed in the hospital over night, and did not come by appointment, were included. Hospital emergency room visits were derived from registers of three public hospitals that count in practice all emergency room visits in the study area. In the emergency room visit data we had cases only for asthma and chronic obstructive pulmonary disease (COPD) visits.

For the definitions of the outcomes we used the codes of International Classification of Diseases 10^{th} revision (ICD-10). For all cardiovascular diseases we used ICD-10 codes I00-I99. We determined the cardiovascular cause-specific effects of pollutants also for coronary heart diseases (I20-I25), myocardial infarctions (I21-I22), arrhythmia (I46.0, I46.9, I47-49), and stroke (I60-61, I63-64). Rest of the ICD-10 codes from classes I00-I99 was determined as "other" cardiovascular diseases. For all respiratory diseases, we used ICD-10 codes J00-J99. The cause-specific respiratory outcomes studied were pneumonia (J12-J15, J16.8, J18), COPD (J41, J44), and asthma (J45, J46). Again, "other" respiratory diseases were determined as the rest of the codes of J00-J99.

To examine whether the population groups differ in susceptibility to air pollutants, the analyses were performed separately for different age groups. However, the analyses were performed for all age groups only if the total number of cases in each analyzed outcome group was $\geq 1\,000$. Age groups were those conventionally used in epidemiological studies; children were those less than 15 years old, adults those aged from 15 to 64 years and the elderly those aged 65 years or older. For adults and the elderly, the hospital admissions and emergency room visits for asthma and COPD were pooled to get a greater number of cases, especially for the emergency room visit analyses. To be consistent between analyses, pooled asthma-COPD data was used also for the hospital admissions. However, for mortality analyses, COPD was analyzed separately, because in the data there were only few deaths due to asthma (101 in total).

4.2 Measurement equipment and sites of pollutants

Particle number counts were measured with a differential mobility particle sizer of the University of Helsinki as described earlier (Hussein et al., 2005). Ten different particle fractions diameter ranging from 0.01 to 0.29 μm were separated and particles less than 0.1 μm in diameter were counted as ultrafine particles. In the beginning of the study period, particle number counts were measured at a bank hill Siltavuori, a 20 meter high peninsula surrounded by urban areas, including downtown Helsinki at the distance of few hundred meters. In March 2001, the measurements started on a hilltop in Kumpula, located 3 km northeast of Siltavuori. In Kumpula, the measurements were conducted on the fourth floor of an office building (20 meters in height) where there is a major highway at a distance of 100 meters. Particle counts at these two sites correlated well with each other (Hussein et al., 2004b). Measurement site change was also taken into account in the statistical analyses by using a dummy variable.

Particle mass measurements ($PM_{2.5}$, PM_{10}) were performed using beta-attenuation method (FH 62 I-R; Eberline Instruments). Carbon monoxide was measured with a non-dispersive infrared monitor (CO-11 M, Environnement SA), NO_2 with continuous monitoring device (Horiba APNA 360, HORIBA International Corp), and SO_2 with automated equivalent method (Thermo Electron Model 43A, Thermo Environmental Instrumentation). In the beginning, the measurements of $PM_{2.5}$, PM_{10}, NO_2, CO, and SO_2 were performed at the same site. Monitors were located in Vallila in a park 14 meters from the closest road. Later (from the beginning of 2004), the particulate mass monitoring was conducted in Kallio at a sports area, where the nearest busy road was 80 m away from the site. These two measurement sites for particles were only one kilometer apart from each other. The mass of coarse particulate matter was obtained ($PM_{10-2.5}$) by subtracting daily levels of $PM_{2.5}$ from PM_{10}. The measurements of SO_2 were only used in the analysis of $PM_{2.5}$ source apportionment.

Ozone was measured (Thermo Environmental Instrumentation Model 49/49C) at a site representing background concentrations in the Helsinki metropolitan area. The site located at a distance of 200 m from the closest busy road and 15 km from the Helsinki city center. The O_3 levels around the measurement site are affected by pollutants from long-range transport, and local traffic. Missing values in the whole air pollution data were replaced with data from measurement sites that were most identical with the primary site, for example the traffic volumes around both sites were similar. The correlation between the 24-h $PM_{2.5}$ and PM_{10} measurements between Kallio and Vallila sites, for example, were 0.95 and 0.93, respectively.

4.3 Confounders; meteorology, influenza and pollen count

Daily meteorological data for the study was gathered from the same locations as particulate mass measurements. As possible confounders in the models we used variables for temperature, relative humidity, and barometric pressure.

We obtained weekly influenza counts from the Infectious Diseases Register of National Institute of Health and Welfare. We created a three-class dummy variable for influenza epidemics by using <35 (cumulative percentage 79), 35–179 (80–94%), and ≥ 180 ($\geq$ 95%) cases per week as the cut points. The influenza data was rightly skewed i.e. the number of those days with no influenza cases at all was large compared to days with influenza cases. This is typical for influenza, since influenza often occurs as epidemics mainly during the cold season. Data with numerous zero value days would have made the continuous influenza variable unsteady.

Daily pollen counts for the six months "pollen period" were derived from the Aerobiology Unit of University of Turku. Pollen measurements in Helsinki were performed on a roof top located approximately 4 km from the particulate measurement sites. Measurements for pollen counts were conducted from the beginning of March to the end of August, which is the pollen period in Finland, each year. Similarly to influenza counts, a dummy for the pollen episodes was created using the daily pollen count sum ≥ 100 of the four most allergenic species (Birch, Mugwort, Alder, Grass) as the cut point.

4.4 Statistical analyses

4.4.1 Time-series analysis

The core models were first built without the air pollutant and the dummy variable for the measurement cite change. Time trend, as continuous variable, and a dummy variable for weekday were always in the models as were variables for the current day mean temperature, relative humidity and barometric pressure. The significance of other confounders, 3 previous days' mean temperature and relative humidity, and the significance of dummy variables for influenza epidemics, high pollen episodes, and general holidays were always checked. These confounders were dropped from the model if their $p>0.20$. The time-series analyses of the associations for the air pollutants with mortality and morbidity were conducted with Poisson regression. The formula for the model used was:

$$\ln[E(y_t)]=a_0+\beta*e_t+\Sigma f_j(x_{tj})+\Sigma\beta_d z_d$$

where y_t= daily number of cases, e=exposure of interest, x=time-varying and z=non-time-varying variables.

In the articles I-III, penalized thin plate regression splines in the generalized additive models (GAMs) framework were used (Wypij, 1996). This method is often used in air pollution time-series studies (Dominici et al., 2002) as many of the confounding parameters, like temperature, are not linear, but can be controlled for with this model better than with ordinary Poisson regression. The linearity of the possible confounding variables in the model was always tested. If the effective degree of freedom for the smooth term for each confounding variable in the model was more than 1.5, the variable was considered to be non-linear. Additionally, plots of the associations between the outcome and the possible confounder were studied to find out whether the association was linear. Smoothing was then applied for all non-linear variables in the final model. Modeling was implemented using R software (2.0.0, 2.6.0 and 2.7.1) (R Development Core Team, 2008), and the mgcv procedure (1.3–7, 1.4–0) (Wood, 2000).

For ozone (article IV), however, the analyses were performed slightly differently. Because there was more autocorrelation in the residuals in the generalized additive model we used robust Poisson regression models that can better control for autocorrelations. The core model was built using a GAM and without the air pollutant. In this model, the long-term time trend was controlled for by dummy variables for each year and month that were always in the model. Other possible confounders were the same as above. Penalized spline smoothing was used to examine the shape of association between weather variables and mortality or morbidity counts, which all turned out to be linear. Finally, the analyses of the associations between ozone and mortality and morbidity were conducted with robust Poisson regression. Robust standard errors of the estimates were used to account for the heteroskedasticity and the observed autocorrelation in the residuals. Modeling was implemented using the Zelig package in R (Imai et al., 2007, 2008) based on the models built using GAM.

The models were built for all outcomes also by warm (May-September) and cold (October-April) season. The division of the seasons was based on the temperature variation in the study area. During the cold season months there were days when temperature dropped below 0°C.

In the models, the 24-hour average concentrations for particulate mass and NO_2, and 24-hour median counts for ultrafine (< 0.1 μm), nucleation (0.01–0.03 μm), Aitken (0.03–0.1 μm), and accumulation (0.1–0.29 μm) mode particles were used. Use of medians for the particle counts was due to the rightly skewed distribution of particles. For O_3 and CO, the 8-hour maximum moving averages were used because the guideline and limit levels for these pollutants are given in this unit following the measurement recommendations by WHO (WHO, 1999), and because of better comparability with previous studies

In advance, it was chosen that analyzes are performed for the effects of zero to five days prior the event, which is a longer period than determined in most previous studies. Averages of lag days 0 and 1 (2-day mean), and lag days 0 to 4 (5-day mean) were also analyzed. Lag 0 is the concentration measured during the 24-hour period from midnight to midnight at the day of event, or in the case of O_3 and CO, the 8-hour maximum moving average concentration at the day of death, hospitalization, or emergency room visit.

Some sensitivity analyses were performed for all models. A partial autocorrelogram of the residuals was used to define the amount of autocorrelation in the residuals and to avoid over-smoothing. Moreover, the analyses were run using the same lag for temperature and the pollutants in the models. In order to study the possible confounding effect of co-pollutants, two-pollutant models were also run for those models that provided significant associations in the single-pollutant analyses. The differences in asthma and asthma-COPD coefficients of pollutants between the age groups and between lag days were tested with a t-test assuming 0 covariance between the coefficients (i.e. using the formula):

$$t = \frac{\beta_1 - \beta_2}{\sqrt{(SE\beta_1)^2 + (SE\beta_2)^2}}$$

Finally, to see whether peak concentrations affected the results, analyses were performed only for days when pollutant concentration was below the 98th percentile of the maximum concentration measured for each pollutant.

4.4.2 Source apportionment of $PM_{2.5}$

Sources of $PM_{2.5}$ were determined using EPA PMF 1.1 model. PMF is an advanced multivariate receptor modeling technique that calculates site-specific source profiles and source contributions (Paatero, 1997). EPA PMF 1.1 solves the general receptor model using constrained, weighted least-squares as implemented in the program ME2 (Paatero, 1999).

Missing, negative and null values in the data were replaced by geometric means of the measures, and these values were weighted down by four. This guaranteed that the replaced value had minor effect on the analysis, but all other values of that day could be used, and no data was missed. The model calculates two matrixes; one combining the sources and pollutants and one combining the power of sources and pollutants. When multiplying these matrixes we got the included pollutants apportioned into different sources.

For source identification, *a priori* knowledge concerning chemical and physical profiles of sources can be used (Grahame and Hidy, 2007; Sarnat et al., 2008). Because

no elemental data was available for this study, factor analysis was performed using daily averages of particulate and gaseous pollutants that are known to originate from emissions of different sources. Models were run assuming three, four, or five factors. The four factor model was found to be physically the most interpretative.

One factor, which was named traffic-related $PM_{2.5}$, was found to be high in $NC_{33\text{-}45}$ (number concentration of particles 33–45 nm in diameter), $NC_{84–114}$ (number concentration of particles 84–114nm in diameter), NO_2, and CO, which indicate traffic-related particles. $NC_{33\text{-}45}$ relates especially to gasoline emissions (Ristovski et al., 1998), while high concentrations of $NC_{84–114}$ indicate diesel emissions (Morawska, 1998).

A second factor was named as soil $PM_{2.5}$, as it was found to have high loading of coarse particles, PM_{10}–$PM_{2.5}$, which indicate particles mainly from soil and road dust, but also particles from sea salt. Particles from soil and re-suspension of road dust, and from other mechanical processes are present mainly in the coarse size fraction (Seinfeld and Pandis, 2006), but they also have a contribution to $PM_{2.5}$.

In Helsinki, SO_2 has been associated with coal/oil combustion (Vallius et al., 2003), and therefore the third factor that was high in SO_2 was named coal/oil combustion $PM_{2.5}$

The fourth factor with high loading of particulate SO_4^{2-} was named as long-range transport $PM_{2.5}$. Secondary sulfate is formed in the atmosphere by oxidation of SO_2 (Grahame and Hidy, 2007) and therefore these particles refer to long-range transport (Niemi et al., 2004). Concentration of particulate SO_4^{2-} was measured at EMEP background station at Virolahti (60°32'N, 27°41'E). Correlation between the Virolahti SO_4^{2-} and Helsinki S was reasonable ($r = 0.75$) for the time period of 2.11.1998–30.4.1999 (unpublished data).

5 RESULTS

We identified 4 sources for $PM_{2.5}$. One factor was formed of secondary sulfate and other long-range transported particles, and the factor's average source contribution was 5.5 µg/m^3 or 57%. The factor describing traffic emissions was characterized by NO_2, CO, $NC_{33–45}$, and $NC_{84–114}$. The average source contribution of traffic factor was 1.8 µg/m3, and it explained, on average, 19% of the $PM_{2.5}$ mass. The average source contribution of the third factor, soil and road dust fraction was 1.0 µg/m^3 (10%). This factor described road dust re-suspended by traffic or wind, and other sources of soil-related or coarse particles. The fourth factor was characterized by SO_2 that, in Helsinki, describes mostly coal combustion emissions and emissions from ship engines that burn residual oil. The average source contribution of the fourth factor was 0.5 µg/m^3 (6%).

The numbers of mortality, hospital admission and emergency room visit counts are given in the original publications (I-IV). The summary of the levels of air pollutants in Helsinki during the whole year, and during warm and cold seasons in 1998-2004 is presented in the Appendix Table 1 of this doctoral dissertation. In addition, the correlations of the pollutants and environmental factors by warm and cold season are provided in the Appendix Tables 2 and 3, and the percent contributions of each $PM_{2.5}$ source to the total $PM_{2.5}$ mass, and the levels of source-specific $PM_{2.5}$ by season are presented in the Appendix Table 4.

In the result tables and figures presented in this dissertation, three particle measures -ultrafine, fine and coarse particles- are presented for the health outcomes where positive associations with particles were observed. These particle fractions were chosen because ultrafine particles describe rather well also the associations observed for nucleation and Aitken mode particles, and results for $PM_{2.5}$ are similar to those found for accumulation mode particles. Comparison of the results to the literature is also more straightforward when using these particulate measures. Presenting the same particle fractions in all figures makes the comparison of the associations between health outcomes and between age groups possible. Some figures also provide additional results –more lag days and different pollutants- to those published in the articles I–IV to give a wider perspective of the findings of this study. All presented results in figures are from one pollutant analyses, and results for 5 lag days are provided.

As a partial overview of the study results, positive findings between ambient particulate pollutants and health effects among the elderly in the whole year analyses and during the warm season are summarized in Tables 4 and 5, respectively. Cold season results are not provided because hardly any associations were observed. A plus mark in the table means that a borderline significant effect or an isolate significant effect was observed. Two plusses mean that there was a strong positive and significant effect observed, and that the association was seen for more than one lag.

Table 4. Summary of the positive associations between particulate matter and cardiorespiratory health among the elderly in 1998–2004 in Helsinki.

Outcome	*Particulate pollutant*			*$PM_{2.5}$ Source*			
	Ultrafine particles	$PM_{2.5}$	Coarse PM	LRT*	Traffic	Soil	Coal/Oil combustion
Mortality							
All cardiovascular							
Stroke					+		
CHD							
Arrhythmia	NA	NA	NA	NA	NA	NA	NA
All respiratory		+	+	+			
Pneumonia		+	+				
COPD							
Hospital admissions							
All cardiovascular			+			+	+
Stroke							
CHD							
Arrhythmia	+				+		
All respiratory		++	+		+		
Pneumonia		++					
Asthma-COPD		++	++	++	+	+	
Other	++	+			+		

* Long-range transport

\+ Isolate significant or borderline significant association

++ Significant (p-value <0.05) and association seen for more than one lag

NA not applicable because number of cases <1000

Table 5. Summary of the positive associations between particulate matter and cardiorespiratory health among the elderly in 1998–2004 in Helsinki during the warm season (May-September).

Outcome	*Particulate pollutant*			*$PM_{2.5}$ Source*			
	Ultrafine particles	$PM_{2.5}$	Coarse PM	LRT *	Traffic	Soil	Coal/Oil combustion
Mortality							
All cardiovascular		+	+			+	
Stroke		++	+	+	++		
CHD							
Arrhythmia	NA	NA	NA	NA	NA	NA	NA
All respiratory		++					
Asthma-COPD	NA	NA	NA	NA	NA	NA	NA
Pneumonia	NA	NA	NA	NA	NA	NA	NA
Hospital admissions							
All cardiovascular	+				+		
Stroke							
CHD			+				
Arrhythmia	+	+			+		
All respiratory		++		+			
Pneumonia		++	++				
Asthma-COPD		++	+				
Other		++	++				

* Long-range transport

\+ Isolate significant or borderline significant association

++ Significant (p-value <0.05) and association seen for more than one lag

NA not applicable because number of cases <1000

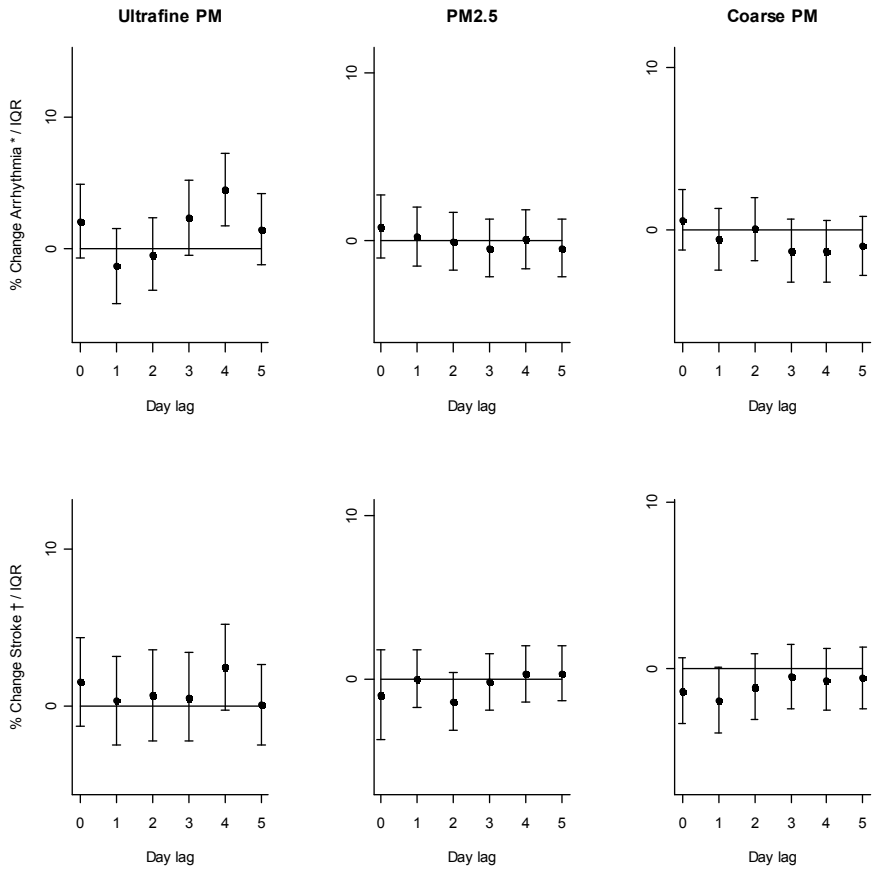
5.1 Cardiovascular health effects of ambient particulate and gaseous pollutants

The associations between ambient air pollutants and cardiovascular mortality and morbidity were determined only for adults and the elderly, because there were an insufficient number of death and admission cases among children.

Consistent positive associations were not found between particulate pollutants and cardiovascular mortality of adults or the elderly in the whole year analyses (article III). Total cardiovascular mortality among the elderly showed positive association only with $PM_{2.5}$ during the warm season with increase of 7.29% (95% CI 1.32–13.6) for 10 μg/m^3. However, a 2 to 3 days lagged negative association was observed between cardiovascular mortality of the elderly and ozone during the warm season (article IV). Among adults, the warm season associations for cardiovascular mortality with particulate mass were mainly negative (Appendix Table 5), but with ozone there was a positive association (article IV). However, the association with ozone was sensitive to adjusting for $PM_{2.5}$.

In the cause-specific mortality analyses, stroke mortality explained the found warm season association between $PM_{2.5}$ and cardiovascular mortality among the elderly (article I). However, in the analyses of hospital admissions, we did not find such an association between stroke and fine particles, but a 2-days lagged negative association was observed for stroke admissions with accumulation mode particles (article III) and with $PM_{2.5}$ (Figure 3).

For cause-specific cardiovascular hospital admissions, the only positive associations with particles were 4 days lagged and found among the elderly. Associations were found for arrhythmia and stroke admissions with ultrafine and Aitken mode particles (Figure 3. article III). However, the associations for arrhythmia and stroke admissions with coarse particles were mainly towards negative direction (Figure 3). Arrhythmia admissions of the elderly were also associated with ozone during the warm season, however, the association was somewhat confounded by $PM_{2.5}$ (article IV).



* Arrhythmia model adjusted for time trend, weekday, holiday, influenza epidemics, temperature (lag 0 and 1–3d mean), relative humidity (lag 0 and 1–3d mean), and barometric pressure

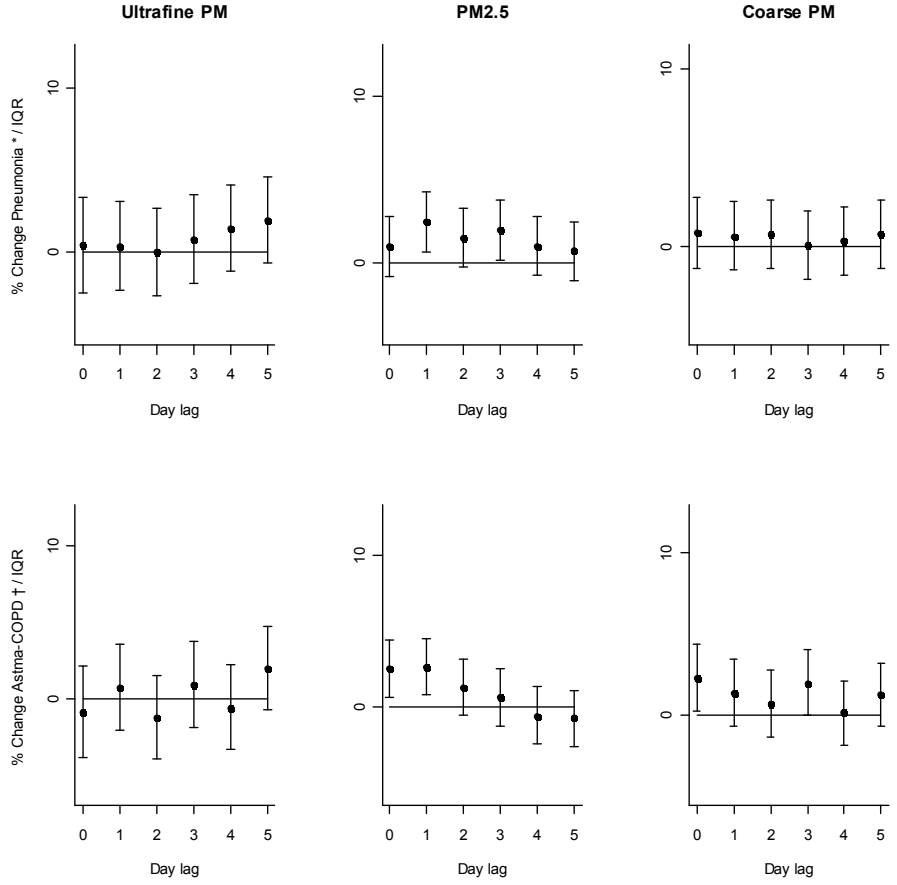
† Stroke model adjusted for time trend, weekday, holiday, temperature (lag 0 and 1–3d mean), relative humidity (lag 0 and 1–3d mean), and barometric pressure

Figure 3. Percent change (95% CI) in arrhythmia and stroke hospital admissions of the elderly for an interquartile increase in ambient particulate pollutants in 1998–2004 in Helsinki.

5.2 Respiratory health effects of ambient particulate and gaseous pollutants

The associations between pollutants and respiratory mortality were determined only for the elderly, because the number of cases was less than 1000 among adults and children. Total respiratory mortality of the elderly was associated with particulate matter at 0 to 1 day lags (article III), and similar effect was found in cause-specific analyses for pneumonia mortality (article III).

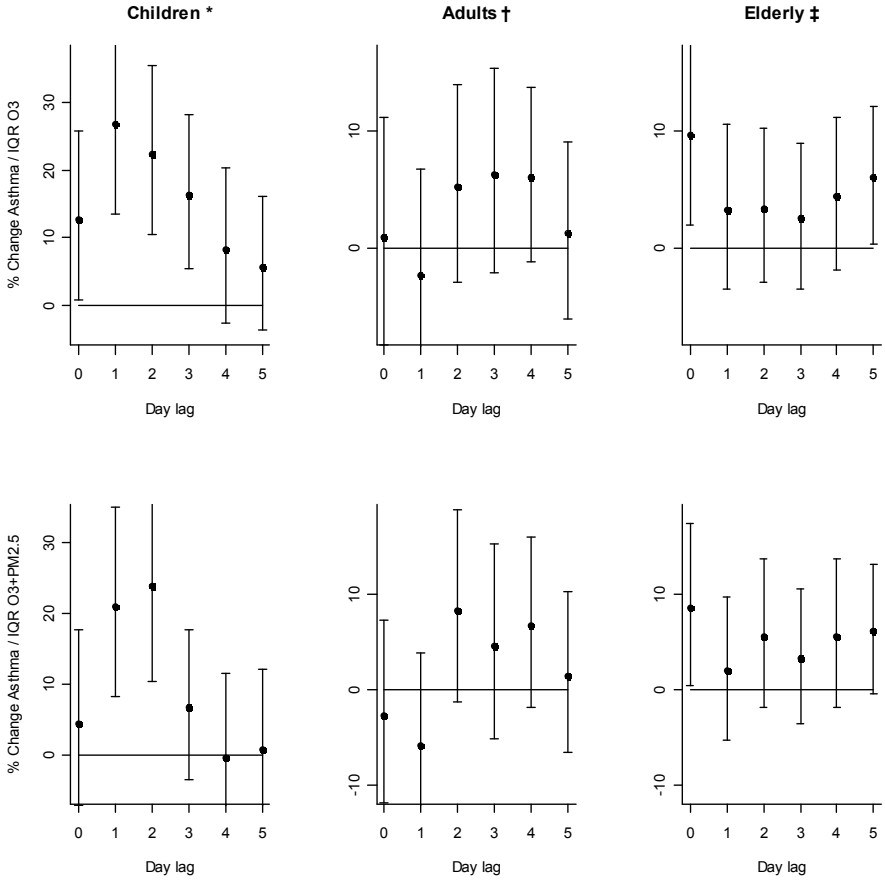
The associations between pollutants and respiratory morbidity were evaluated using hospital admission and hospital emergency room visit counts. These analyses were performed for all three age groups. All respiratory, pneumonia, and asthma-COPD hospital admissions as well as asthma-COPD emergency room visits of the elderly were associated with four different particulate fractions, namely Aitken, accumulation, and coarse mode particles, and $PM_{2.5}$, and also with CO in the whole year analyses (articles II and III). In Figure 4, associations for three of the particle fractions with pneumonia and asthma-COPD hospital admissions of the elderly are presented. During the warm season, associations between particulate pollutants and respiratory admissions of the elderly were generally stronger than in the whole year analyses (article III). Ozone had also positive association with asthma-COPD admissions of the elderly during the warm season (article IV and Figure 5).



* Pneumonia model adjusted for time trend, weekday, influenza epidemics, temperature (lag 0), relative humidity (lag 0), and barometric pressure

† Asthma-COPD model adjusted for time trend, weekday, influenza epidemics, high pollen episodes, temperature (lag 0), relative humidity (lag 0 and 1–3d mean), and barometric pressure

Figure 4. Percent change (95% CI) in pneumonia and asthma-COPD hospital admissions of the elderly for an interquartile increase ambient particulate pollutants in 1998–2004 in Helsinki.

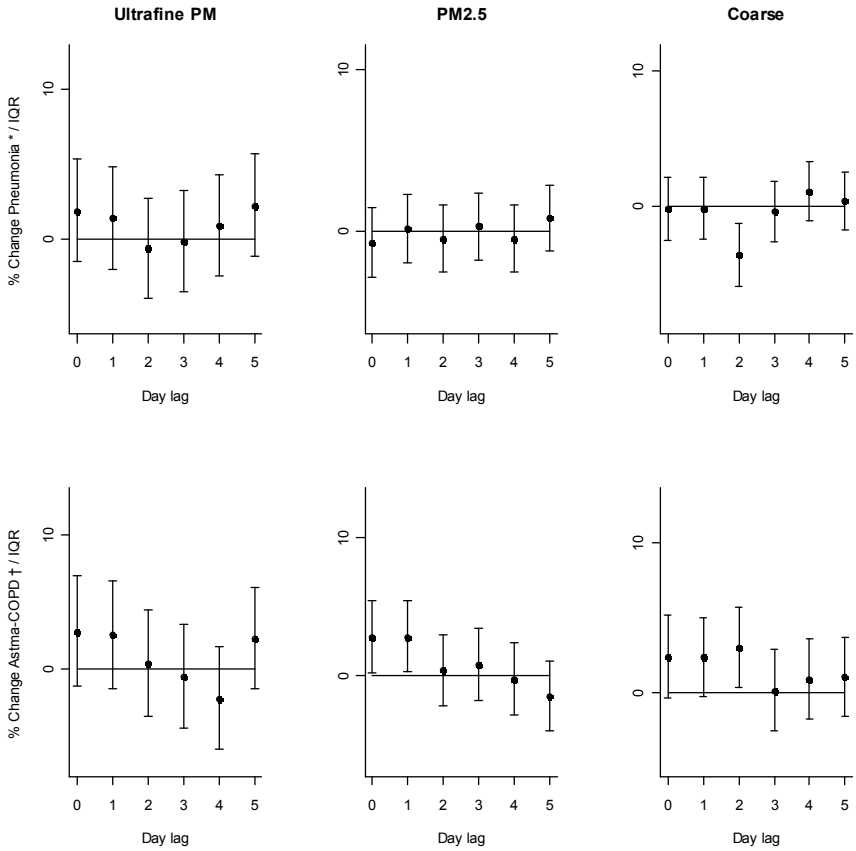


* Model for children adjusted for year, month, weekday, holiday, high pollen episodes, temperature (lag 0), relative humidity (lag 0), and barometric pressure

† Model for adults adjusted for year, month, weekday, holiday, high pollen episodes, temperature (lag 0), relative humidity (lag 0), and barometric pressure

‡ Model for the elderly adjusted for year, month, weekday, high pollen episodes, temperature (lag 0), relative humidity (lag 0 and 1–3d mean), and barometric pressure

Figure 5. Percent change in emergency room visits for asthma among children, and in hospital admissions for asthma-COPD among adults and the elderly for an interquartile change in O_3 in single pollutant model and in model adjusted to $PM_{2.5}$ in 1998–2004 in Helsinki.



* Pneumonia model adjusted for time trend, weekday, holiday, influenza epidemics, temperature (lag 0 and 1–3d mean), relative humidity (lag 0 and 1–3d mean), and barometric pressure

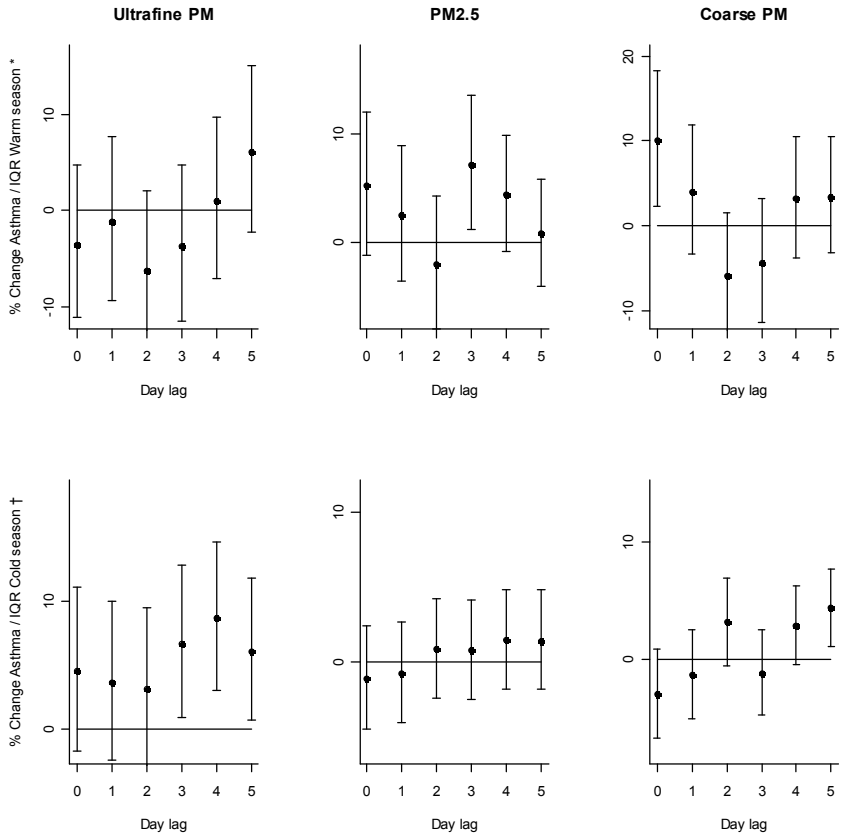
† Asthma-COPD model adjusted for time trend, weekday, influenza epidemics, high pollen episodes, temperature (lag 0), relative humidity (lag 0 and 1–3d mean), and barometric pressure

Figure 6. Percent change (95% CI) in pneumonia and asthma-COPD hospital admissions of adults for an interquartile increase in ambient particulate pollutants in 1998–2004 in Helsinki.

We observed only few positive associations between particulate pollutants and all respiratory hospital admissions of adults. However, both asthma-COPD admissions and emergency room visits among adults were positively, although non-significantly, associated with changes in the current and previous-day levels of all particulate measures (article II and Figure 6). There was also a negative association between pneumonia admissions among adults and coarse particles at lag 2 (Figure 6).

Among children, increases in $PM_{2.5}$ and coarse mode particle levels increased hospital admissions for all respiratory diseases during the whole year, and the warm season (Appendix

Table 6). However, coarse particles had positive association also with all respiratory hospital admissions and asthma emergency room visits during the cold season (Appendix Table 6 and Figure 7). Strong associations were found in the whole year analyses between asthma emergency room visits and traffic-related pollutants; ultrafine particles, NO_2 and CO (article II). In the season-specific analyses for children, the association between ultrafine particles and asthma visits emerged during the cold season. $PM_{2.5}$ and coarse particles had positive association with asthma visits during the warm season, however, associations were observed at different lags (Figure 7). Ozone had also a strong association with the asthma visits of children during the warm season (article IV and Figure 5).



* Warm season model adjusted for time trend, weekday, holiday, influenza epidemic, high pollen episode, temperature (lag 0 and 1–3d mean), relative humidity (lag 0 and 1–3d mean), and barometric pressure

† Cold season model adjusted for time trend, weekday, holiday, influenza epidemics, temperature (lag 0 and 1–3d mean), relative humidity (lag 0 and 1–3d mean), and barometric pressure

Figure 7. Percent change (95% CI) in asthma emergency room visits of children for an interquartile increase in ambient particulate pollutants during warm and cold season in 1998–2004 in Helsinki.

Two-pollutant analyses were run as sensitivity analyses to see if other pollutants have confounding effect on the associations observed. Nitrogen dioxide seemed to confound the associations of ultrafine particles. The results for the single- and two-pollutant analyses for asthma and asthma-COPD emergency room visits among children and the elderly, respectively, are provided in Table 6. The presented lags are those where strong positive associations were observed for particulate measure in single-pollutant analyses, i.e. 2-d mean for the elderly where significant association with $PM_{2.5}$ was observed, and lag day 4 for children where significant association with ultrafine particles was observed.

Table 6. Percent change (95% Confidence Interval) in emergency room visits for asthma–COPD among the elderly and asthma among children for an interquartile increase in pollutants, in 1998–2004. Results for single– and two–pollutant models.

	Single Pollutant Model	With CO	With NO_2	With ultrafine particles	With $PM_{2.5}$	With Coarse PM
Asthma-COPD Elderly (2-d mean)						
Ultrafine particles	2.64 (–1.28–6.71)	0.87 (–3.29–5.20)	–0.52 (–5.30–4.50)	–	2.14 (–1.47–5.88)	1.96 (–2.16–6.24)
$PM_{2.5}$	3.32 [a] (0.93–5.76)	2.68 [a] (0.16–5.326	2.52 [b] (–0.09–5.21)	3.10 [a] (0.55–5.72)	–	3.18 [a] (0.66–5.76)
Coarse PM	1.90 (–0.64–4.51)	1.30 (–1.28–3.96)	0.92 (–1.79–3.71)	1.41 (–1.21–4.10)	0.83 (–1.84–3.58)	–
Asthma Children (Lag 4)						
Ultrafine particles	6.06 [a] (2.34–11.0)	6.22 [a] (1.59–11.1)	–0.98 (–6.11–4.62)	–	6.16 [a] (1.66–10.9)	6.59 [a] (2.08c11.3)
$PM_{2.5}$	2.56 [b] (–0.17–5.36)	0.19 (–0.10–0.47)	0.00 (–0.30–0.29)	1.44 (1.44–4.41)	–	1.20 (–1.72–4.22)
Coarse PM	1.21 (–1.67–4.17)	0.57 (–2.38–3.61)	–1.97 (–5.04–1.21)	0.75 (–2.24–3.83)	0.86 (–2.17–3.99)	–

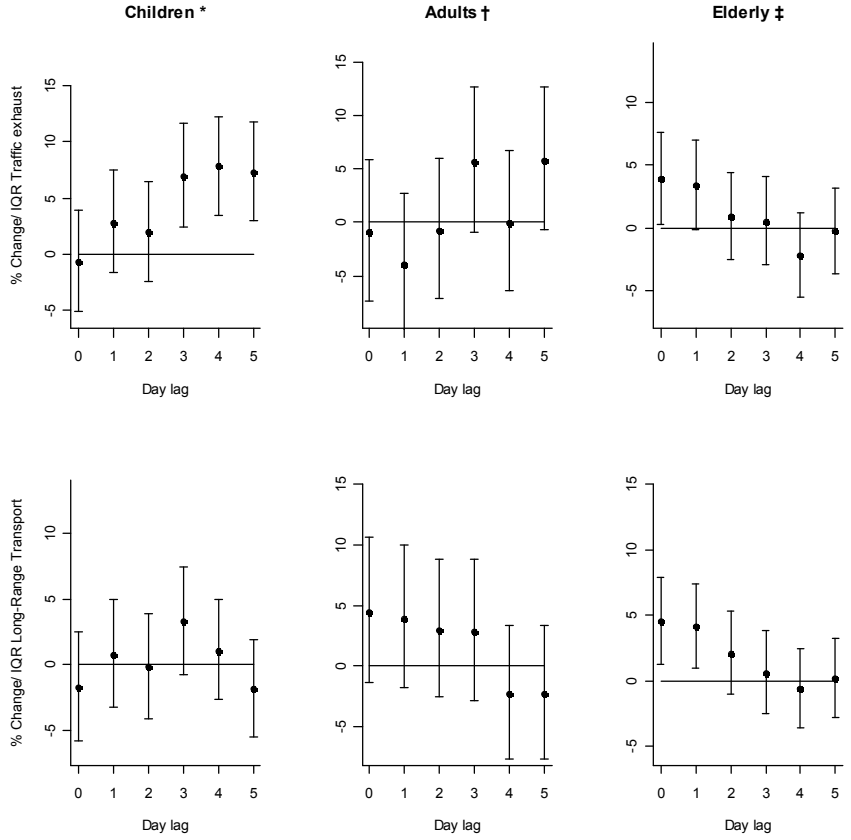
[a] $p<0.05$

[b] $p<0.10$

5.3 Health effects of source-specified $PM_{2.5}$

Cardiovascular outcomes were not associated with source apportioned $PM_{2.5}$, as there were few associations between cardiovascular health and particulate matter in general (article III). Total respiratory mortality and morbidity of the elderly had positive associations with $PM_{2.5}$ from long-range transport, traffic and soil (article III). Particles derived from the same three sources had positive, though non-significant, associations also with asthma-COPD morbidity of the elderly and adults (articles II and III, Figure 8). Traffic-related particles had a strong and delayed association with exacerbation of asthma in children (article II, Figure 8). Figure 8 presents the associations observed for $PM_{2.5}$ from traffic and

long-range transport with the emergency room visits for asthma among children and for asthma-COPD among adults and the elderly. Particles from these two sources had more significant associations with respiratory morbidity than soil or coal and oil combustion particles.



* Model for children adjusted for time trend, weekday, influenza epidemics, high pollen episodes, temperature (lag 0 and 1–3d mean), relative humidity (lag 0 and 1–3d mean), and barometric pressure

† Model for adults adjusted for time trend, weekday, influenza epidemics, high pollen episodes, temperature (lag 0 and 1–3d mean), relative humidity (lag 0), and barometric pressure

‡ Model for the elderly adjusted for time trend, weekday, influenza epidemics, high pollen episodes, temperature (lag 0), relative humidity (lag 0 and 1–3d mean), and barometric pressure

Figure 8. Percent change in emergency room visits for asthma among children, and for asthma-COPD among adults and the elderly for an interquartile change in traffic-related and long-range transported $PM_{2.5}$ in 1998–2004 in Helsinki.

6 DISCUSSION

The current study compared the effects of air pollutants on cardiovascular and respiratory mortality and morbidity in the Helsinki metropolitan area, Finland. Respiratory health effects were stronger and more consistently observed than cardiovascular effects. All of the particle size fractions had some harmful health effects, accumulation mode particles and $PM_{2.5}$ having most often adverse effects. Of the source-specified particles traffic-related and long-range transported but also soil derived particles showed adverse health effects. It was also was found that children under 15 years of age and people aged ≥ 65 are somewhat more sensitive to the effects of ambient air pollutants than adult population.

6.1 Cardiovascular versus respiratory health effects of ambient particulate pollutants

6.1.1 Morbidity: hospital admissions and emergency room visits

In the current study, it was shown that ambient air pollutants have harmful effects on respiratory health in Helsinki metropolitan area; however, there is less evidence about associations between pollutants and cardiovascular outcomes. One of the most significant findings of this study was the association between asthma exacerbation in children and traffic-related pollutants (article II, Figures 7 and 8). The associations for asthma visits with ultrafine particles, NO_2 and $PM_{2.5}$ from traffic were strong and consistently three to five days lagged. However, because these pollutants are closely correlated (Appendix Tables 2 and 3), and the association of ultrafine particles became weaker and non-significant in two-pollutant model with NO_2 (Table 6), we could not specify the causal component of traffic emissions that is responsible for the observed effect. Previously, traffic-related pollutants have been associated to health decrements in panel studies of asthmatic children in Kuopio (Pekkanen et al., 1997; Timonen and Pekkanen, 1997). In the APHEA study, asthma hospital admissions of children were heterogeneously associated with the levels of NO_2, and in Helsinki asthma admissions were not affected by NO_2 (Sunyer et al., 1997). However, the current study period was longer compared to APHEA study and therefore there was more power in the statistical analyses in the current study. The emergency room visit data used in this study may also be more sensitive than previously used hospital admission data, resulting in greater effect estimates. In general, our findings add to the cumulative evidence in support of the association between exposure to traffic-related air pollutants and respiratory health of children (Andersen et al., 2008; Andersen et al., 2007a; Barnett et al., 2005; Peel et al., 2005).

Among the elderly, respiratory morbidity was linked to increases in ozone and ambient particulate pollutants in different size fractions. Studying either hospital admission or emergency room visit data resulted in similar associations (articles II, III, and IV, Figures 4 and 5). However, there were little associations between cardiovascular hospital admissions and ambient particles (article III). Greater effects on the respiratory than on cardiovascular health have been reported also by Anderson et al. (2001). In more recent studies, the effects on cardiovascular and respiratory health have been found comparable (Host et al., 2008; Peng et al., 2008).

In the current study, accumulation mode particles had a strong association with all respiratory diseases among the elderly, however, the same day effect was similar to that of $PM_{2.5}$ (2.4%, 0.06–4.83, for 10 μg m^{-3}) and coarse particles (1.7%, –0.16–3.59 for 10 μg m^{-3}) (article III). The associations for accumulation mode or fine particles were independent of other pollutants, only minor changes in the effect estimates were observed after adjusting to co-pollutants (Table 6 and appendix of article III). Even though the levels of $PM_{2.5}$ in Helsinki are low compared to other European cities and metropolises, as strong associations for respiratory diseases have rarely been reported elsewhere. In comparison, increases in all respiratory disease admissions in association with $PM_{2.5}$ among the elderly population have been 0.8% (95% CI –2.8–4.5, lag 0) in Canada (Fung et al., 2006), –0.7% (95% CI –2.4–1.1, 2-d mean) in the United Kingdom (Anderson et al., 2001), 0.0% (95% CI –9.8–10.8, 5-day mean) in Denmark (Andersen et al., 2008), and 0.5% (95% CI –2.0–3.0, 2-d mean) in France (Host et al., 2008). However, in the study of Anderson et al. (2001) there was little evidence of any associations between air pollutants and morbidity, and the authors suggested that this was due to shortness of the time-series, or due to the small variance in the air pollution levels. In Denmark, on the other hand, the association had not been seen for $PM_{2.5}$ but for accumulation mode particles and PM_{10}. The association between accumulation mode particles and respiratory admissions of the elderly (4.0%, 95% CI 0.0–8.2 for 495 change in number count over 4-day mean) (Andersen et al., 2008) was similar to the current findings.

In the cause-specific analyses, accumulation mode particles and $PM_{2.5}$ were more strongly associated with pooled asthma-COPD admissions than with all respiratory admissions among the elderly (article III). The association found between $PM_{2.5}$ and COPD alone (9.2% (4.0–14.6), at lag 0) is comparable to those reported earlier from Detroit (Ito, 2003), and Vancouver (Chen et al., 2004). The associations between particles and respiratory health outcomes of the elderly were also stronger during the warm than during the cold season (article III). This may be due to the better exposure assessment during the warm season when people tend to be more active and spend more time outdoors. The ventilation through open windows is also more common in the summer than in winter, which leads to better exposure assessment to ambient particles. Greater warm season

(Medina-Ramon et al., 2006; Peng et al., 2005), but also cold season (Bell et al., 2008) effects of air pollution have been reported earlier. Differences between studies may reflect differences in particulate compositions, and in city specific characteristics such as climate (Medina-Ramon et al., 2006).

Cause-specific cardiovascular admissions had only weak associations with particulate pollutants, which were mainly due to arrhythmia cases. This finding is somewhat inconsistent with the evidence of cardiovascular effects of particulate pollutants reported previously from Helsinki (Lanki et al., 2006a; Pekkanen et al., 2002; Timonen et al., 2006; von Klot et al., 2005). The inconsistency between the current and previous morbidity studies may partly derive from different study populations included to the analyses. Earlier, a study by von Klot et al. (2005) included a cohort of people with a history of diagnosed cardiac event, and Pekkanen et al. (2002), Lanki et al. (2006a) and Timonen et al. (2006) studied a panel of patients with stable coronary heart disease. Therefore, it is possible that cardiovascular effects of ambient particles in Helsinki are seen only among the more susceptible individuals, such as those with some underlying cardiorespiratory disease.

6.1.2 Mortality

All respiratory and pneumonia mortality of the elderly were also associated with particulate air pollution (article III). A significant association was observed between all respiratory mortality and accumulation mode particles (5.06% / IQR 287, at lag 1) the fraction that is closely correlated with $PM_{2.5}$. Even though no earlier studies have determined the associations between respiratory mortality and size-specified particles, respiratory mortality of the elderly has correspondingly been linked to changes in ambient $PM_{2.5}$ (Franklin et al., 2007; Goldberg et al., 2001b). In Helsinki, inhalable particles, PM_{10}, have also been linked to increased respiratory mortality in the total population (Penttinen et al., 2004).

The associations between cardiovascular mortality and ambient particulate matter or ozone were again weaker than associations observed for respiratory mortality (articles III and IV). Conclusions that support this finding for particles have been reported in two earlier studies (Pope et al., 1992; Wichmann et al., 2000). However, recently a finding where the effects of particles on cardiovascular health were stronger than on respiratory health was also reported (Ostro et al., 2007).

In the current study, all cardiovascular mortality among the elderly had a positive association with the current-day $PM_{2.5}$ only during the warm season. This association was explained in the cause-specific analyses by stroke mortality (article I). However, because there was also a negative association between stroke hospital admissions and $PM_{2.5}$ (Figure 3, article III), the usability and comparability of the mortality and hospital

admission registers for stroke is discussed in more detail in the section 6.1.3.

Particulate air pollution has been associated with cardiovascular health decrements in numerous epidemiological studies worldwide (Table 1). The approximate increase in cardiovascular mortality in association with 10 μg m^{-3} increase in $PM_{2.5}$ has been estimated to be 1% (Pope and Dockery, 2006). Such an association was not observed in Helsinki. The reasons for the inconsistent findings from the current study compared to the majority of previous literature are difficult to determine. One explanation can be that the composition of fine particles in Helsinki differs from that elsewhere in Europe or in North America. Long-range transported particles account for about half of the fine particle mass in Helsinki (Kulmala, 2000; Vallius et al., 2003), and during the transportation, particles may go through chemical reactions in the atmosphere that possibly convert them into less toxic forms. Thus it can be speculated that the irritating and inflammatory effects of particles would explain the observed respiratory effects, even if the particles were less toxic, but they would not be strong enough to affect the cardiovascular system. There is already some evidence that the local differences in the health effects are due to different particle components (Bell et al., 2009), however, there are no studies that would have shown that more toxic particles are required for the cardiovascular than for respiratory effects. Other reasons could be the smaller variation in the particulate levels, and somewhat worse exposure assessment to ambient pollutants in Helsinki compared to warmer countries and cities. In Finland, ventilation through windows is uncommon during long and cold winters, and houses in general are built tight, which decreases the exposure to ambient particles. During the cold season the impact of indoor sources on personal exposure may also be higher (Brown et al., 2008). The worse exposure assessment would affect especially the whole year and cold season effect estimates, which is supported by the current findings where stronger associations for the respiratory outcomes were observed for the warm season analyses compared to whole year analyses (article III).

6.1.3 Comparison between morbidity and mortality analyses

In this study, data on daily mortality, hospital admission, or emergency room visit counts were used. Most of the analyses were performed for only one or two data bases, because of the lack of data (emergency room visit data available only for asthma and COPD), or the low number of cases (e.g. mortality among adults and children). For those outcomes where analyses were run for different data bases, the main conclusions from the analyses were mainly the same. However, for some endpoints, especially stroke, also clear differences were observed, as discussed below.

For all respiratory causes, conclusions on associations with mortality and hospital admissions were similar in the sense that for both outcomes a significant association with

accumulation mode particles and with $PM_{2.5}$ was found on the current day (article III). For all respiratory admissions, significant associations were found for several lag days, but for mortality only the association at lag 0 was significant. This difference between mortality and morbidity analyses may be due to the fact that more severe exacerbation of disease is needed for a death than an admission to take place. Because the proportion of population that suffers from respiratory outcomes leading to admissions is larger than the population suffering from mortality, the more severe outcome (Figure 1), admission analyses have more statistical power, which is likely to lead to more significant associations.

Analyses for all three data bases (mortality, hospital admission, and emergency room visit) were only performed for asthma-COPD among the elderly. However, in the mortality analyses only deaths for COPD were included. Here again mortality and morbidity analyses showed similar positive associations with $PM_{2.5}$ and accumulation mode particles at lag days 0–1 (Figure 4, articles II and III). The strongest associations were found for asthma-COPD emergency room visits (article II), and the weakest associations for COPD mortality (article III). It seems that emergency room visit data is more sensitive to describe changes in morbidity than hospital admission data. This is possibly because the emergency room visit data includes all acute asthma-COPD event seeking emergency care, also the less severe ones, but to be counted as an admission the subject needs to stay in hospital over night. In addition, patients presenting late in the evening are more likely to stay overnight in the hospital, although the severity of their attack may be comparable to a patient presenting early in the morning and leaving on the same day. The lower number of COPD deaths compared to exacerbations may again have resulted in weaker associations in the mortality analyses. It therefore seems that emergency room visit data describes better the associations of ambient pollutants with acute exacerbation of asthma and COPD than hospital admissions or mortality and should be favored in the future studies.

In both, mortality and hospital admission analyses for pneumonia among the elderly, associations with accumulation mode particles and $PM_{2.5}$ were found (article III). However, a difference in the associations was that for mortality significant association was found on the same day, whereas for admissions significant associations were found at lag day 1 and over the 5-d mean. The difference in the effect lag may be explained by the behavioral reasons. People may wait at home a day or two for the disease to get more severe before seeking medical help from hospitals, which is why the associations for pneumonia admissions occur at later lags than associations with mortality.

Mortality and morbidity data bases for all cardiovascular diseases and coronary heart disease among the elderly were consistent in the sense that both data sets provided mainly small effect estimates that were not significant (article III).

The largest inconsistency between mortality and morbidity analyses was found for stroke, where mortality was positively (article I) and morbidity negatively associated with

$PM_{2.5}$ (Figure 3 and article III). The negative association between stroke admissions and $PM_{2.5}$ is consistent with the results of a Taiwanese study (Chan et al., 2006). However, we do not know what the reason for the negative association is, or whether it is an association found by chance. It seems valid to suggest that elderly patients who have suffered from stroke form a vulnerable population group that may then suffer from pneumonia and other diseases ending in hospitalization and finally in death. Thus the diagnosis for the hospitalization (and immediate cause of death) may be registered as something else than stroke, but the underlying cause of death, used in the current mortality analyses, in the register may be stroke. Therefore there is possibly some overlap in the data used for stroke mortality and for stroke hospital admissions and the current results for mortality and admissions are not fully comparable. Future studies should combine fatal and non-fatal strokes on an individual level to provide more information about the mechanism of action of particulate matter on stroke.

In the present study, it was possible to use an exceptionally wide array of registers and outcomes. The study showed that using different registers and several disease outcomes in the same study is useful, and it provides a wider perspective on the health effects of ambient pollutants. Although mostly, the results from analyses using different registers gave similar conclusions on the acute health effects of ambient pollution, also some severe differences were observed, mainly for stroke. Therefore, before embarking on new register-based time series studies, the investigators should carefully scrutinize the validity of the register data to be used in the light of the hypothesis to be tested. When possible, like in the Nordic countries, several registers should be combined to get a more complete, non-overlapping data on mortality and morbidity.

6.2 Role of particle size fractions and $PM_{2.5}$ sources

The source apportionment of $PM_{2.5}$ via positive matrix factorization analysis in the current study provided information on the same sources as earlier principal component analysis performed for Helsinki $PM_{2.5}$ data (Vallius et al., 2005; Vallius et al., 2003). Only sea salt could not be separated as its own factor because of the lack of suitable marker elements. However, the average source contributions were in the range of earlier results (Vallius et al., 2005; Vallius et al., 2003). Due to the long time period (2 557 days) the model was stable and therefore considered valid for the apportionment of sources. The method has also been found to be comparable with other source apportionment methods (Thurston et al., 2005).

Traffic-related $PM_{2.5}$ and ultrafine particles, a marker of traffic-related particles, were now investigated in separate models. Stronger associations were observed for asthma exacerbation among children with ultrafine particles (6.3% / IQR (5 700) increase in UFP

over the 5-d mean) than with larger particles, and with traffic-related $PM_{2.5}$ than $PM_{2.5}$ from other sources (article II). The associations for traffic-related pollutants at lags 4 and 5 were also statistically different from the associations at lag 0. This suggests that fresh local particles among other traffic emissions are harmful especially for the respiratory system of children and that the response among children is not acute. However, because the effect of ultrafine particles was very similar to those of NO_2 and CO, and because the association for ultrafine particles was changed in two-pollutant model with NO_2 (Table 6), these results suggest that it is the mixture of traffic-related pollutants causing the effects. The strong effect of NO_2 on asthma visits of children suggests that especially NO_2 is a good marker of traffic-related emissions, which is consistent with previous findings (WHO, 2005). Only two other studies have investigated associations between asthma and ultrafine particles in a time-series setting. Andersen et al. (2008) reported very identical findings compared to the current results. Peel et al. (2005) studied also the effects of ultrafine particles on asthma emergency room visits. The results were in agreement with the current findings: associations were stronger among children than among adults, and the strongest effects were observed to be 5 to 8 days delayed. However, this study had incomplete data of ultrafine particles with 44% days of missing data. In several other studies, particles related to traffic have also been suggested to be the most harmful for health (Gold et al., 2005; Laden et al., 2000; Metzger et al., 2004; Ostro et al., 2007; Sarnat et al., 2008).

For the other health outcomes and age groups, however, the difference between the effects of different particle fractions or $PM_{2.5}$ sources was not that clear. Exacerbation of all respiratory diseases, pneumonia, and asthma-COPD among the elderly, and asthma-COPD among adults were associated with several particulate fractions and sources (articles II and III, Figures 4 and 6). In many previous studies black smoke or black carbon have been shown to have strong effects on health outcomes (Analitis et al., 2006; Bremner et al., 1999; Schwartz et al., 2005). These pollution measures are markers of carbon containing particles that are emitted from various combustion sources. As we were lacking the elemental data of the particles for our source apportionment analysis, we could not separate the causal components of particles. This means that harmful particle components such as elemental carbon are possibly included in several, if not in all, source categories determined in this study, and therefore adverse effects are seen in more than one source category.

All the associations found among older age groups were the strongest at lags 0 to 2 days (articles II and III) and therefore different from those found among children (article II). However, even though the effects seem acute, there is also some cumulative effect of particles among the elderly as the effect estimates for some of the particle measures over the 5-day mean were higher than those for the individual lags (article III).

The strongest associations among the elderly were observed between respiratory

morbidity and accumulation mode particles that mainly originate from long-range transport (articles II and III). Similar associations have been reported earlier by Penttinen et al. (2006) and Andersen et al. (2008). Peters et al. (1997) have also suggested that particles in both ultrafine and accumulation mode size fractions have effects on the respiratory health among asthmatic adults. Accumulation mode particles are mostly secondary particles, which have also been linked to increased respiratory and cardiovascular morbidity elsewhere (Sarnat et al., 2008).

The lack of clear and independent associations between particles in the ultrafine size fraction and health outcomes, and stronger associations found for $PM_{2.5}$ and accumulation mode can be a result of differences in the exposure assessment. Exposure assessment of ultrafine particles is poorer compared to fine particles. This is due to the local variation in ultrafine particle concentrations, and the poor penetration ability of these particles to indoor environments (Koponen, 2001). As people, especially adults and the elderly, spend most of their time indoors they may actually be rarely exposed to fresh ultrafine particles. It is possible that the individual effects of ultrafine particles are difficult determined in population level studies where central site measurements are used as proxies to personal exposure.

Even though clear differences between the effects of particle sources were not found in this study, it seems that traffic is one of the most harmful emission sources of ambient pollutants in Helsinki, and also elsewhere (Gold et al., 2005; Laden et al., 2000; Metzger et al., 2004; Ostro et al., 2007; Sarnat et al., 2008). It cannot be differentiated however, based on these results, which of the individual traffic-related pollutants is responsible for the health effects in Helsinki. This is partly due to the current lack of particulate component data. It is supposed that it is the mixture of pollutants, rather than a single pollutant that causes the observed health effects in the airways. Part of this mixture, contributing especially to the mass of fine particles, is also formed of non-exhaust particles derived from car brakes, traffic road abrasion, and re-suspended road dust (Thorpe and Harrison, 2008), and the possible health effects of the non-exhaust particles have not been evaluated so far. However, traffic exhaust pollutants are those whose emissions are being regulated, and we can try to avoid exposure to them. The portion of long-range transported particles in Helsinki, on the other hand, cannot be regulated or limited only by local actions. Therefore, to avoid the health effects of these particles, the international vehicle emission restrictions such as Euro 5 and 6 (The EEA Joint Committee, 2007) should be fulfilled also in other European countries and in Russia from where the particles are transported to Finland.

The Euro 5 and 6 standards are one of the measures designed to reduce emissions of particulate matter and ozone precursors such as nitrogen oxides and hydrocarbons. These standards are based on the findings of health risks reported in the CAFÉ Programme

(European Union, 2005). The standards are needed, but it takes tens of years to regenerate the whole car pool that is currently in use. Because the reductions of the traffic-related emissions via new technologies slowly improve the air quality, we should now pay attention to the exposure patterns of traffic-related air pollutants.

6.3 Does age matter?

There were clear differences between the effects of ambient particles on asthma and COPD emergency room visits found among children and older people. Among the elderly and adults the associations were observed for accumulation mode particles, $PM_{2.5}$, and coarse particles at lag days 0 to 2 (Figure 4, articles II and III), but among children there were associations with traffic emissions, including ultrafine particles, with 3 to 5 days delay (Figure 6 and article II). At lag 4, the effect of traffic-related pollutants on the asthma visits among children was statistically significantly different from adults and the elderly (article II). The reason for the different lag structures can be due to different effect mechanisms between different particle fractions; ultrafine particles can penetrate deeper into the lung than fine particles (Donaldson and Stone, 2003), and their clearance from the airways is slower than that of larger particles (Kreyling et al., 2006). Therefore, ultrafine particles may cause inflammation in the lower airways and lung tissues, and time from the induction of inflammation cascade to the actual observable effect may be longer. Larger particles, however, deposit mainly on the upper region of the respiratory system (Schulz, 2000) and may cause irritation and epithelial disruptions that might induce exacerbation of respiratory illnesses with shorter delay.

The size of the harmful particle fraction also differed between age groups. Ultrafine particles, with other traffic-related pollutants, had stronger associations than larger particles among children (Figure 6, article II) whereas larger particles; accumulation mode particles, $PM_{2.5}$, and coarse particles had more associations among the elderly (Figure 4, article II). This difference between age groups can be related to the differences in the exposure and in the exposure assessment of pollutants, which derives from different time activity patterns between children and older people. Children are active and known to spend more time outdoors than adults (Klepeis et al., 2001; Liu et al., 2003), and therefore they presumably get also more exposed to short-lived ultrafine particles and other traffic emissions. Adults may more often work in air conditioned office buildings than other population groups, which diminishes their exposure to ambient pollutants, and especially the exposure to ultrafine particles (Koponen, 2001). Healthy adults may also be biologically the least sensitive group to the effects of air pollution. Their respiratory system is fully developed and they are not yet suffering from chronic diseases or other reductions in the defense mechanisms in the airways as the elderly often do.

6.4 Acute health effects of ambient ozone

In addition to particulate pollutants, asthma among children and asthma-COPD among the elderly were exacerbated after exposure to ozone during the warm season (article IV and Figure 5). The association between ozone and respiratory outcomes seemed to be independent of $PM_{2.5}$ (Figure 5) and even stronger than that of $PM_{2.5}$, which could derive from the high oxidative capacity of ozone. Associations between ozone and respiratory morbidity have been reported also in numerous epidemiological studies elsewhere (Babin et al., 2007; Ko et al., 2007; Medina-Ramon et al., 2006; Moore et al., 2008; Spix et al., 1998; Szyszkowicz, 2008).

Even though the association between ozone and mortality has been well established in several multi-city studies from Europe, North America, and Asia (Bell et al., 2005; Gryparis et al., 2004; Ito et al., 2005; Levy et al., 2005; Wong et al., 2008), and once in Helsinki (Penttinen et al., 2004), such associations were not observed in the current analyses. There was a positive association between ozone and cardiovascular mortality among adults when the model was adjusted for $PM_{2.5}$. However, the association with ozone was not significant in the single-pollutant model (article IV). Adjusting for $PM_{2.5}$ affected also the association observed between ozone and arrhythmia admissions among the elderly. After adjusting the model for $PM_{2.5}$, the effect estimate for ozone was smaller than in single-pollutant model, and non-significant (article IV). It is possible that some confounding occurs between O_3 and $PM_{2.5}$ in Helsinki, because much of both pollutants is long-range transported. In line with this is the suggestion that O_3 would be a surrogate for secondary particles or $PM_{2.5}$ exposure (Sarnat et al., 2001).

There was also a negative association between ozone and cardiovascular mortality among the elderly. There is no clear explanation for this, but it can be speculated that on hot days, when ozone concentrations are high, the elderly people stay indoors and therefore they are less exposed to ambient pollutants, and the effect turns to negative.

The levels of ozone in Helsinki exceed the air quality guideline level (100 $\mu g\ m^{-3}$, 8-hour mean) set by WHO (WHO, 2005) few times each year, and the mean levels of ozone have been slowly increasing, rather than decreasing, during the last decade. It is noteworthy that the health effects were observed already at the current levels, because ozone levels are expected to increase in the future because of the global warming (Patz et al., 2005). Warmer climate may accelerate ozone formation and therefore increase the ambient levels of this pollutant. Local formation of ozone in Helsinki may also increase. This is partly because of the increasing trend of using diesel-driven cars with the current technology that leads to larger emissions of ozone precursor gases such as NO_2 than emissions from petrol-driven cars. At the same time, there is a decreasing trend in the levels of traffic-related particles and thus there are less ozone sinks i.e. pollutants consuming ozone. Overall, limiting the

vehicle emissions is a double-edged sword because the reduction of emissions of particles and emissions of ozone precursor gases are difficult to be implemented at once.

6.5 Validity considerations

The data measurements of this study were carefully performed, and the measurement period of ultrafine particles was longer than in previous studies (Peel et al., 2005; Wichmann et al., 2000). It is also unique that ambient particles were continuously measured in several size fractions making it possible to study different particle fractions separately. The health data in this study was also of good quality. The data for this study was derived from national registers where all diseases were coded by the International Causes of Diseases 10th revision codes. National Causes of Death Register in Finland has been maintained since the 1969. The current form of National Hospital Discharge Register has been maintained since 1987, but similar, though not as accurate, information has been collected already from the 1969. Validity of the National Causes of Death and Hospital Discharge Registers in Finland has been shown to be good at least for stroke (Tolonen et al., 2007), coronary heart disease (Pajunen et al., 2005), and myocardial infarction (Rapola et al., 1997). Even though the data quality of this study is good and the methods used are commonly accepted, there are some weaknesses in this study that are discussed below.

In environmental epidemiology, the problem of possible confounding by several environmental variables is always present. In this study, the effects of weather variables were controlled by the models used. Confounding of ambient co-pollutants is also possible, and therefore some two-pollutant models were run in this study. It was found that NO_2 has some confounding effect on the associations of particulate pollutants, especially on the associations of ultrafine particles (Table 6 and article III). However, because the levels of NO_2 and CO in Helsinki are low, these are considered more of markers of their source, which is mainly traffic, rather than causal pollutants. Because NO_2 seemed to confound the association of ultrafine particles, and because there is lack of biological plausibility for the effects of gaseous pollutants, it is difficult to determine the causal pollutant that is responsible for the observed effects among children. Some confounding was also observed between ozone and $PM_{2.5}$ (article IV). When adjusting the ozone model to $PM_{2.5}$, the association between ozone and cardiovascular mortality among adults became stronger, but the association between ozone and arrhythmia admissions of the elderly became weaker (article IV). However, the 2-pollutant models may not be able to separate the effects of individual pollutants because of the correlations of pollutants originating from the same source, and findings that some pollutants are acting as surrogates for personal exposure to fine particles from mobile sources (Sarnat et al, 2001).

One possible limitation of the study is the validity of the exposure assessment. Exposure

assessment to ambient pollutants would be best evaluated with personal monitoring of pollutants. However, this would show the true exposure only if the ambient and non-ambient origin particles were also separated. Personal measurements are not possible for population level studies such as time-series studies because of their high costs, and therefore measurement campaigns have been performed to evaluate the usability of central site measurements as proxies to personal exposure in the study area. Because most of the fine particle mass in Helsinki is long-range transported (Kulmala et al., 2001; Vallius et al., 2003), the concentrations are not too heavily affected by the local particle sources. It has been shown that the central site measurements for $PM_{2.5}$ are valid to be used as proxies for personal exposure in epidemiological studies (Pekkanen and Kulmala, 2004). Indoor and outdoor concentrations of $PM_{2.5}$ are also highly correlated in Helsinki (Hoek et al., 2008; Janssen et al., 2005), which indicates that the variation in personal exposure to these particles is comparable to the measured variation in ambient levels. However, the correlations between indoor-outdoor concentrations of particle number and PM_{10} are lower (Hoek et al., 2008). The correlation between ultrafine particle counts at different outdoor measurement sites in Helsinki has been found to be moderate (Aalto et al., 2005; Buzorius et al., 1999; Hussein et al., 2004b).

A possible source of exposure misclassification in this study may also be the time lag used. The air pollutants were measured from midnight to midnight, and the death and morbidity counts were daily. Thus if the event occurred at 1 a.m., for example, it is not lag 0, but lag 1 that describes the exposure 24-hours preceding the event. Because we analyzed several lag days, it is reasonable to assume that none of the effects was missed. However, we did not have the times of deaths, admissions or emergency room visits for more accurate grouping of exposure, which possibly leads to some random misclassification and attenuation the observed effects.

Data collection for this study was performed over the years 1998–2004. The particulate and gaseous pollutant measurements were available for the whole study period. However, the locations of particulate mass and particle number count measurement sites changed once during the study period. The measurement site change was taken into account in the statistical analyses so that it would not affect the results.

In this research, an extensive number of statistical analyses were performed using a variety of air pollutant measures, health outcomes, several time lags, and three different age groups. All this testing may have led to some significant effects that were due to chance. Therefore more focus is put on those findings where the effects are consistent. This means that there is a trend in the effect lag structure showing a biologically plausible effect, and that the effect is similar over several related exposures and outcomes.

6.6 Suggestions for future studies

This study had an extensive data, and numerous analyses were performed, but there is still need for further studies. There was a lack of the elemental data on the particle compositions in the current study, which is why the portion of sea salt in the $PM_{2.5}$ mass could not be separated like it had been done in the previous study by Vallius et al. (2003). For the same reason, the mass of non-exhaust traffic particles, or particles that are derived from biomass combustion could neither be apportioned. To apportion the particles from the biomass combustion there should have been measurements of markers of wood combustion such as levoglucosan (Simoneit et al., 1999). Apportionment of particle sources with data including elemental particle composition could also better reveal differences between the health effects by particle sources.

There is increasing interest in studying the health effects of particles from biomass combustion. For example, in a recent animal study, particles from wood combustion were shown to have an almost equal allergy adjuvant effect than particles from traffic sources (Samuelsen et al., 2008), and a chamber study showed that exposure to wood smoke increases the levels of airway inflammation markers (Barregard et al., 2008). In Helsinki metropolitan area, wood is used as a secondary heat source in 58% of the residences (Haaparanta et al., 2003), and therefore the use of fireplaces probably produces a considerable portion of the ambient fine particle mass especially during the cold season. However, little is known about the health effects of the particles from wood and biomass combustion, and more research on the particle sources generally is still needed to specify more clearly the most harmful particles.

Little associations were observed for cardiovascular outcomes in this study and one of the suggested reasons was that the components of particles in Helsinki are different from other studies. A measurement campaign that would enable determination of the components of particulate matter would make possible the comparison of the PM component data in Helsinki to data from other cities. This could provide evidence for the hypothesis that there are differences in the particulate compositions between study locations. Additionally, the health effects on cardiovascular outcomes could be more precisely studied in analyses by particulate components.

In the current study, the individual effect of ultrafine particles could not be shown, but their effect was related to traffic emissions as a whole. To further study the role of specified particle fractions or individual pollutants, panel and chamber studies are needed. In panel studies, there is possibility to assess personal exposure more accurately than in time-series studies, which makes the analyses more reliable. If different pollutants can be personally monitored at the same, the confounding effects of co-pollutants could also be addressed. So far, there are only a few panel studies determining the effects of ultrafine particles (Ruckerl

et al., 2006). In chamber studies, exposure to pollutants could be controlled for, and exposure to a specified pollutant could be studied (Samet et al., 2007). This way the exclusion of the possible confounding effects of co-pollutants would also be possible. However, there are some limitations when considering these study methods. In both cases, there can be only small number of cases included, and the costs are high. Moreover, in the chamber studies one can only study health subjects and health outcomes that are reversible.

We do not know how much the validity of exposure assessment actually differs between age groups. Therefore there remains also need for panel studies measuring and comparing personal exposure among children, adults, and the elderly. Personal measurements and time-activity diaries could provide evidence for the argument that the negative association observed between cardiovascular mortality and ozone during the warm season is really due to the habit of elderly staying indoors on hot days therefore exposing less to ambient pollutants. Another way to study why this negative effect was found could be stratification of the data by temperature instead of season.

It is possible that using the 24-hour average concentrations for the pollutants in time-series studies masks the possible effects of shorter exposure peaks. Studies using shorter time scale for the pollutant measurements, and health data including the time of onset of the health outcome could be able to reveal such short-term associations.

As we were not able to link mortality and morbidity data on an individual level, some overlap between the data sets occurs in the current study. The linkage between the two data would make the separate determination of the effects of air pollutants on in- and out-of-hospital mortality possible (Forastiere et al., 2005).

In this study, three sub-populations were studied to find out the vulnerable age groups. To further explore possibly vulnerable sub-populations, medical history of sub-populations could be used. Diabetics and asthmatics, for example, have been suggested to be more vulnerable to the effects of air pollution (Sarnat and Holguin, 2007; Zanobetti and Schwartz, 2001). Another way to determine susceptible population groups is the study of gene-environment interactions. Studies where blood samples are drawn from the study subjects such as cohort or panel studies, could exploit the available technologies to assess the differences in the human genome. Then also the associations between polymorphism and environmental stressors could be studied. A number of important gene-environment interactions have already been identified, and the interactions suggest that the involved genetic variation is suggestive of certain underlying effect mechanisms (von Mutius, 2009).

Finally, the health effects studied here were short-term effects. Following a cohort of people from Helsinki would make it possible to study the health effects of long-term exposure to air pollutants. So far no Finnish cohorts have studied the health effects of air pollution.

7 CONCLUSIONS

The main conclusions from this study are In Helsinki, there are consistent associations between ambient air pollutants and respiratory health, but there is less evidence about the association between air pollutants and cardiovascular health. Previous international studies and panel studies from Helsinki suggest the importance of particulate matter in Helsinki, but the cardiovascular effects are possibly seen only among more vulnerable population groups such those with an underlying cardiorespiratory disease.

There are some differences in the health effects of ambient particles in different size fractions. Particles in the accumulation mode (0.1–0.3 μm) that very well describe the mass of particles with diameter <2.5 μm have more associations with different respiratory outcomes than other particle fractions, especially among the elderly. These associations are 0–2 days lagged. Ultrafine particles (<0.1 μm), among other markers of traffic, have more delayed association with the exacerbation of asthma among children. However, in this study it was not possible to identify the causal component of traffic emissions responsible for the observed effects. Among older age groups investigated, the poorer exposure assessment of ultrafine particles may have caused the lack of such associations.

Traffic-related particles seem to cause stronger health effects than particles from other sources among children. Among the elderly and adults, particles from traffic and long-range transport, but also from soil are harmful. The difficulty to separate the effects between sources may be due to the distribution of the causal components of ambient particles to different source fractions, e.g. the harmful carbon components can be found in both the traffic and long-range transported particles. The particle components could not be determined from the data in use.

The effects of particulate pollutants on respiratory health are greater among children and the elderly than among adults. This may be a result of the greater vulnerability of children because of the developmental stage of their respiratory system, and the greater amount of inhalation compared to their body mass than among older people. Vulnerability of the elderly may derive from biologically decreased pulmonary function or other underlying diseases. Another reason for the differences between age groups can be the exposure patterns with children probably experiencing the most exposure especially to ultrafine particles and other traffic-related pollutants.

Among children, ozone and traffic-related pollutants, including ultrafine particles, have a strong effect on asthma exacerbation. Reductions in the exposure to traffic-related pollutants that are also precursors of ozone, should be aimed mainly by reducing emissions through city planning, increased use of public transport, and by improved engine design. In

addition, to decrease the health effects of these pollutants we should diminish the exposure to them by avoiding outdoor activities near heavy trafficked roads. In the town planning, the location of day care centers, schools, and nursing homes should not be in the vicinity of highly trafficked roads. In those buildings in close vicinity to roads, the air filtration should be well arranged.

Among the elderly, ozone and particles in different size fractions have detrimental effects on respiratory health. The effects are seen especially as exacerbation of asthma-COPD and pneumonia. The harmful particles are mainly derived from long-range transport, soil and traffic. Therefore the reduction of ambient air pollutant emissions not only locally, but also globally would be necessary.

The results underline the importance of particulate matter together with ozone as a main environmental threat to health also in Helsinki.

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APPENDICES

Appendix Table 1. Summary of particulate mass and gaseous pollutant concentrations, and number counts of particles by season in, 1998–2004 in Helsinki.

Nucleation mode (< 0.03 µm) (1 cm^{-3})	Min	25%	Mean	75%	Max	Sd
Whole year	379	2673	4859	6256	22790	3168
Warm season	412	2215	3682	4844	12970	1916
Cold season	379	3162	5701	7324	22790	3591
Aitken mode (0.03–0.1 µm) (1 cm^{-3})						
Whole year	400	2470	4000	4937	27990	2264
Warm season	570	2734	3936	4796	11820	1695
Cold season	400	2286	4045	5017	27990	2596
Ultrafine particles (< 0.1 µm) (1 cm^{-3})						
Whole year	914	5780	9273	11540	50990	5137
Warm season	1819	5616	8068	10000	21340	3344
Cold season	914	5989	10130	12830	50990	5958
Accumulation mode (0.1–0.29 µm) (1cm^{-3})						
Whole year	57	238	417	525	2680	260
Warm season	68	244	423	549	1839	242
Cold season	57	235	412	512	2680	272
$PM_{2.5}$ (µg m^{-3})						
Whole year	1.1	5.5	9.5	11.7	69.5	5.9
Warm season	1.1	5.3	8.8	11.0	41.5	5.0
Cold season	1.1	5.6	9.9	12.3	69.5	6.4
Coarse PM, $PM_{10-2.5}$ (µg m^{-3})						
Whole year	0.0	4.9	9.9	12.1	101.4	8.3
Warm season	0.0	6.1	9.5	11.8	42.0	5.1
Cold season	0.0	4.2	10.2	12.5	101.4	9.9
O3 (µg m^{-3} 8-hour max moving average)						
Whole year	1.6	49.6	63.0	76.6	159.1	20.0
Warm season	16.3	58.6	71.3	84.1	159.1	17.9
Cold season	1.6	44.0	57.1	68.8	130.6	19.4
NO_2 (µg m^{-3})						
Whole year	3.4	20.1	28.2	34.3	96.4	11.3
Warm season	3.4	19.3	26.5	32.7	66.8	10.0
Cold season	5.9	20.9	29.4	35.5	96.4	12.1
CO (mg m^{-3} 8-hour max moving average)						
Whole year	0.1	0.3	0.5	0.6	2.4	0.22
Warm season	0.1	0.3	0.4	0.5	1.1	0.16
Cold season	0.1	0.4	0.5	0.6	2.4	0.25

Appendix Table 2. Spearman rank correlations between air pollutants and environmental factors during the warm season in 1998–2004 in Helsinki.

	NUC	AIT	ACC	PM_{25}	PMC	TRAF	LRT	SOIL	COAL	NO_2	O_3	CO	TEMP	RH	Bp
UFP	0.89	0.89	0.30	0.29	0.47	0.74	0.04	0.46	0.37	0.59	0.09	0.39	–0.15	–0.17	0.15
NUC		0.60	0.04	0.04	0.36	0.68	–0.17	0.34	0.16	0.43	–0.07	0.37	–0.30	–0.21	0.10
AIT			0.46	0.43	0.47	0.66	0.21	0.46	0.50	0.62	0.20	0.33	0.01	–0.07	0.15
ACC				0.90	0.38	0.18	0.76	0.43	0.34	0.47	0.45	0.18	0.49	0.17	0.08
PM_{25}					0.40	0.19	0.81	0.46	0.30	0.47	0.43	0.23	0.43	0.17	0.10
PMC						0.28	0.25	0.99	0.36	0.47	0.38	0.21	0.02	–0.33	0.24
TRAF							–0.08	0.29	0.04	0.54	–0.06	0.68	–0.11	0.01	0.06
SEC								0.25	0.21	0.25	0.42	0.08	0.38	0.30	–0.02
SOIL									0.33	0.49	0.40	0.21	0.07	–0.33	0.26
COAL										0.52	0.20	0.03	0.02	–0.14	0.21
NO_2											0.08	0.36	0.03	–0.02	0.20
O_3												–0.06	0.28	–0.34	0.09
CO													0.01	0.13	0.05
TEMP														0.02	0.08
RH															–0.40

Nuc = nucleation mode particles, diameter <0.03m, Ait = Aitken mode, 0.03–0.1m, Accu = Accumulation mode, 0.1–0.29 µm, PMC = coarse PM, $PM_{10\text{-}2.5}$, Traf = Traffic $PM_{2.5}$, LRT = Long range transported $PM_{2.5}$, Soil = Soil $PM_{2.5}$, Coal = Coal and oil combustion $PM_{2.5}$, Temp = Temperature, RH = Relative humidity, Bp = Barometric pressure

Appendix Table 3. Spearman rank correlations between air pollutants and environmental factors during the cold season in 1998–2004 in Helsinki.

	NUC	AIT	ACC	PM_{25}	PMC	TRAF	SEC	SOIL	COAL	NO_2	O_3	CO	TEMP	RH	Bp
UFP	0.94	0.91	0.40	0.37	0.18	0.75	0.15	0.15	0.46	0.67	–0.09	0.47	–0.30	–0.13	0.11
NUC		0.74	0.20	0.19	0.12	0.66	0.01	0.10	0.33	0.58	–0.08	0.40	–0.35	–0.16	0.07
AIT			0.58	0.52	0.20	0.76	0.30	0.17	0.56	0.69	–0.11	0.49	–0.19	–0.05	0.16
ACC				0.87	0.11	0.32	0.79	0.11	0.45	0.33	–0.12	0.30	0.05	0.16	0.14
PM_{25}					0.19	0.22	0.83	0.20	0.52	0.33	–0.01	0.31	–0.09	–0.02	0.20
PMC						0.12	–0.01	0.99	0.13	0.26	0.32	0.06	0.19	–0.51	0.22
TRAF							–0.05	0.11	0.19	0.68	–0.21	0.66	–0.06	0.04	0.08
SEC								–0.03	0.38	0.08	–0.01	0.14	–0.06	0.16	0.11
SOIL									0.10	0.26	0.32	0.05	0.20	–0.51	0.22
COAL										0.48	–0.11	0.24	–0.37	–0.13	0.22
NO_2											–0.11	0.47	–0.20	–0.07	0.20
O_3												–0.24	0.11	–0.50	0.01
CO													–0.12	0.07	0.03
TEMP														0.05	–0.03
RH															–0.28

Nuc = nucleation mode particles, diameter <0.03m, Ait = Aitken mode, 0.03–0.1m, Accu = Accumulation mode, 0.1–0.29 µm, PMC = coarse PM, $PM_{10\text{-}2.5}$, Traf = Traffic $PM_{2.5}$, LRT = Long range transported $PM_{2.5}$, Soil = Soil $PM_{2.5}$, Coal = Coal and oil combustion $PM_{2.5}$, Temp = Temperature, RH = Relative humidity, Bp = Barometric pressure **Appendix**

Appendix Table 4. The average percent contributions of the identified sources to $PM_{2.5}$ mass, and concentrations of source-specified $PM_{2.5}$ by season in, 1998–2004 in Helsinki.

$PM_{2.5}$ Source ($\mu g\ m^{-3}$)	% of $PM_{2.5}$	Min	25%	50%	75%	Max
Long-range transport	57					
Whole year		0	2.5	5.5	7.3	30.8
Warm season		0	2.2	4.8	6.4	20.7
Cold season		0	2.7	6.0	8.1	30.8
Traffic	19					
Whole year		0	1.2	1.8	2.3	7.4
Warm season		0	1.3	1.8	2.3	5.0
Cold season		0	1.2	1.9	2.4	7.4
Soil and Road dust	10					
Whole year		0	0.5	1.0	1.2	10.7
Warm season		0	0.6	0.9	1.2	6.0
Cold season		0	0.4	1.0	1.2	10.7
Coal / Oil combustion	6					
Whole year		0	0.2	0.5	0.7	11.3
Warm season		0	0.2	0.4	0.6	3.1
Cold season		0	0.3	0.5	0.8	11.3

Appendix Table 5. Percent change in cardiovascular mortality among adults for an Interquartile change in ultrafine particles, $PM_{2.5}$, coarse particles, and ozone during the whole year and by season in 1998–2004 in Helsinki.

	Whole year			Warm season			Cold season		
	N = 3 029			N = 1 292			N = 1 737		
	% change	95% CI		% change	95% CI		% change	95% CI	
UFP									
Lag 0	0.82	–4.46	6.40	0.63	–3.46	4.90	0.37	–6.82	8.12
Lag 1	–2.64	–7.66	2.65	–2.05	–5.97	2.04	–0.35	–7.07	6.85
Lag 2	–4.69 †	–9.51	0.39	–3.64	–7.42	0.30	–3.03	–9.42	3.81
Lag 3	–3.26	–8.04	1.77	–2.53	–6.27	1.36	–1.39	–7.75	5.41
Lag 4	–1.40	–6.19	3.63	–1.08	–4.81	2.79	1.65	–4.78	8.50
Lag 5	0.43	–4.35	5.45	0.33	–3.37	4.18	4.29	–2.15	11.2
$PM_{2.5}$									
Lag 0	1.18	–2.06	4.54	–0.20	–6.91	7.00	2.63	–1.24	6.64
Lag 1	–0.89	–4.07	2.39	–5.70	–11.6	0.60	1.66	–2.18	5.65
Lag 2	–1.50	–4.65	1.76	–3.01	–8.92	3.28	–1.02	–4.87	3.00
Lag 3	–3.67 *	–6.84	–0.40	–7.97 *	–13.7	–1.83	–2.08	–5.97	1.96
Lag 4	–1.50	–4.65	1.75	–5.68 †	–11.2	0.22	0.77	–3.09	4.77
Lag 5	–0.50	–3.65	2.75	–6.80 *	–12.2	–1.05	3.11	–0.71	7.06
Coarse PM									
Lag 0	–0.77	–4.40	3.01	–6.35	–14.9	3.11	2.16	–2.21	6.72
Lag 1	–1.39	–4.95	2.31	–1.40	–9.87	7.87	–0.03	–3.96	4.06
Lag 2	–3.37	–6.94	0.35	–4.82	–13.0	4.13	–2.49	–6.45	1.64
Lag 3	–2.06	–5.50	1.51	–10.6 *	–18.3	–2.23	0.63	–3.15	4.55
Lag 4	–1.68	–5.01	1.77	–8.83 *	–16.4	–0.57	0.59	–3.17	4.50
Lag 5	–3.20	–6.56	0.29	–11.6 *	–18.9	–3.66	–0.38	–4.25	3.64
O_3									
Lag 0	–3.35	–10.2	4.06	4.44	–7.85	18.4	–8.32 †	–17.0	1.28
Lag 1	–2.07	–8.63	4.95	6.90	–3.79	18.8	–7.82 †	–16.1	1.31
Lag 2	1.75	–4.76	8.70	1.63	–8.08	12.4	1.11	–6.98	9.91
Lag 3	–0.52	–6.67	6.05	–3.55	–12.3	6.11	1.46	–6.87	10.5
Lag 4	–3.70	–9.56	2.53	–0.61	–9.33	8.94	–6.71	–14.2	1.44
Lag 5	–3.03	–9.10	3.45	–2.01	–11.2	8.15	–4.21	–12.0	4.32

* $p<0.05$

† $p<0.10$

Appendix Table 6. Percent change in all respiratory hospital admissions of children for an Interquartile range increase in ultrafine particles, $PM_{2.5}$, and coarse particles by season in 1998–2004 in Helsinki.

	Whole year			Warm season			Cold season		
	N = 2 147			N = 894			N = 1 253		
	% change	95% CI		% change	95% CI		% change	95% CI	
UFP									
Lag 0	0.78	–1.96	3.60	–0.68	–6.27	5.24	2.06	–1.42	5.66
Lag 1	0.74	–1.93	3.48	2.68	–3.19	8.92	–0.01	–3.18	3.28
Lag 2	–0.25	–2.88	2.46	–2.86	–8.34	2.96	0.09	–2.97	3.25
Lag 3	0.32	–2.22	2.93	–1.74	–7.29	4.16	0.07	–2.97	3.20
Lag 4	–0.49	–2.92	2.01	0.96	–4.72	6.98	–0.79	–3.78	2.29
Lag 5	–2.20 †	–4.57	0.23	0.77	–4.76	6.62	–3.55	–6.47	–0.54
$PM_{2.5}$									
Lag 0	2.15 *	0.36	3.97	4.25 †	–0.13	8.83	1.42	–0.49	3.37
Lag 1	2.01 *	0.29	3.77	4.87 *	0.69	9.22	1.34	–0.53	3.24
Lag 2	0.40	–1.32	2.14	–2.03	–6.01	2.13	0.79	–1.07	2.68
Lag 3	0.20	–1.52	1.94	–0.38	–4.26	3.67	0.23	–1.64	2.14
Lag 4	–1.48	–3.15	0.22	–4.65	–8.16	–1.02	–0.58	–2.45	1.32
Lag 5	–1.48	–3.11	0.19	–4.36	–7.67	–0.93	–0.38	–2.24	1.51
Coarse PM									
Lag 0	1.70	–0.21	3.63	2.45	–1.41	6.47	2.39 *	0.29	4.54
Lag 1	0.46	–1.43	2.40	3.73 *	0.04	7.55	0.36	–1.74	2.51
Lag 2	1.24	–0.64	3.16	0.69	–3.01	4.54	2.24 *	0.12	4.40
Lag 3	0.21	–1.62	2.07	–0.56	–4.18	3.20	1.14	–0.87	3.20
Lag 4	0.58	–1.18	2.37	0.39	–3.09	3.98	1.33	–0.59	3.27
Lag 5	–1.03	–2.77	0.75	–0.08	–3.43	3.37	–0.42	–2.33	1.52

* $p<0.05$

† $p<0.10$